

# HydroGlobe

*Definition of a global  
framework for hydrotherapy*



*A FEMTEC - FoRST joint project with the cooperation of  
ISMH and the technical support of WHO  
(World Health Organization)*

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## **INTRODUCTION**

Millions of people around the world use hydrotherapy (HT). Such widespread use, especially in South America, East Asia and Africa, has led to increased professional and public debate across the world on HT as a form of healthcare.

In the main European Countries, HT training is incorporated into medical curricula and HT treatments are provided by national healthcare systems. However, commonly accepted definitions of HT therapies and products are yet to be established.

**FEMTEC** ([www.femteconline.org](http://www.femteconline.org)) is one of the most representative medical thermal HT associations, having been founded in 1937. It has official working relations with the World Health Organization (WHO). Together, they develop programmes using natural resorts for therapy and health. FEMTEC is a co-promoter of the WHO-GARD (Global Alliance against Chronic Respiratory Diseases) international programme ([www.who.int/respiratory/gard/en/](http://www.who.int/respiratory/gard/en/)). The Federation maintains close contacts with international medical hydrology associations like **ISMH** (International Society of Medical Hydrology, [www.ismh-direct.net](http://www.ismh-direct.net)), universities and ministries of health in different countries.

**FoRST** ([www.fondazioneforst.it](http://www.fondazioneforst.it)) is the Italian Foundation, established in 2003, for scientific research on HT. It provides funding for scientific research in hydrology and balneotherapy. FoRST is practically the sole provider of funding for research in this research area in Italy.

FoRST recently redesigned its own system for evaluating scientific projects. As such, to ensure funding goes to the best projects, the decision was taken to follow standard, internationally-recognized project evaluation procedures using external experts as peer reviewers.

Even if HT is growing and ever more widespread, there is still a significant lack of data in this field, no list of the different types of HT and the definitions have not yet been finalized. In addition, the legal status of these therapies and the training programmes vary drastically from country to country. There is still no international assessment of the use of this kind of therapy.

## **CHALLENGES TO EXPAND SAFE AND EFFECTIVE ACCESS AND USE OF HT AROUND THE WORLD**

Despite the growth in the knowledge of HT, in many European countries there are problems evaluating the efficacy of HT treatments and, consequently, in promoting their proper use. For public policy makers to fund therapies, they need more and clearer evidence. Indeed, a lack of

information has meant that, in some cases, the relevant authorities are struggling to decide whether or not to finance such therapies. Consumers also find it hard to get advice on how and when to use the HT.

In addition, local health authorities are finding it troublesome to identify qualified HT providers. The sheer scope of HT exacerbates these problems.

However, it is not only Europe that is grappling with these issues. Governments and health authorities in Russia, Latin America, China, the Far East and North Africa face similar issues, as the use of complementary medicine and HT have also grown considerably in these parts of the world in recent years.

## **HYDROTHERAPY (HT) AND TRADITIONAL MEDICINE (TRM)**

Over many years and in a number of documents HT has been grouped under TRM<sup>1</sup>. Since 2007, HT has been a reference point in the TRM/CAM Team at WHO's Geneva headquarters.

## **WHO TRADITIONAL MEDICINE STRATEGY 2002-2005**

WHO's Traditional Medicine Strategy 2002-2005 had four major objectives:

- to integrate TRM with national healthcare systems, as appropriate;
- to promote the safety, efficacy and quality of TRM, by expanding the TRM knowledge base;
- to increase the availability and affordability of TRM, as appropriate;
- to promote the therapeutically sound use of appropriate TRM, by both providers and consumers.

## **AIMS OF THIS PROJECT**

- Define HT
- Describe HT methodologies and their mechanisms of action
- Provide relevant data on the use of HT in several countries
- Explore the legal status of HT in several countries

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<sup>1</sup> WHO, *WHO-TRM Strategy 2002-2005*, WHO Geneva, 2002, available online at: <http://apps.who.int/medicinedocs/en/d/Js2297e/> visited on 14 May 2013

- Select and bring together available scientific data on HT, concerning its efficacy, safety and proper use, so as to build a global framework for the use of HT
- Provide the World Health Organization with monitoring survey and legal status data so it can evaluate the HT use framework

## **PREFACE**

An understanding of the historical background and the place of HT in the "heritage" of medical knowledge used by mankind over thousands of years to meet health need requires a comprehensive understanding of the history and development of HT since the arrival of the scientific research methodology. Consequently, this work looks at the historical development of these treatments, the most common therapeutic indications and the descriptions of their effects on the body. Furthermore, between August and December 2012, a systematic review of scientific literature, articles and research papers from Medline was undertaken. The results showed that HT is an age-old therapy that has changed significantly over time. It slowly developed from a largely passive role, where the key element was simply bathing, to having an active role. Increasingly, water has been used with innovative methods and with therapeutic indications based more and more on scientific research. Despite this, there is no general consensus on many aspects of this method. HT is mainly used to treat respiratory, bone-joint and vascular conditions. However, it can have beneficial effects on the entire human body, through the use of spa water (localized or systemic), inducing the body to activate homeostasis that, in turn, leads to natural stabilization. It is precisely this adaptogen element, which in many ways is non-specific, that generates more questions and doubts, and therefore necessitates of more in-depth research.

More specifically, some key questions still do not have definitive answers:

1. How does this medicine define itself and how is it used by the public across the world?
2. How effective is HT? What are the benefits and risks?
3. What is the legal status of HT and how is it organized across the world?
4. How is HT used and what are the main methodologies adopted? What are its main indications?

## **METHODOLOGIES**

To grasp the full complexity of this form of medicine, we chose a multidimensional approach (medical, sociological, legal and



organizational). We used appropriate methods for each of these dimensions:

- a systematic description of the historical sources and of the several methodologies for applying this medical branch;
- a systematic review of the scientific literature to evaluate the clinical efficacy and safety of HT;
- a detailed analysis of the legal and organizational framework and its ramifications;
- broad-based consultation with professional associations and experts to describe how HT is organized and how practitioners are trained in each country;
- the creation, dissemination and collection, through individual experts in the various countries, of Monitor Survey Data so as to assess the status of this medicine in the different countries that have a long and documented tradition of using it or that are in the process of introducing it into their healthcare systems;
- recognition of the legal status in some countries.
- Combined, such data creates a picture of the current status of HT in some countries, but they cannot provide a complete answer to the initial research questions because of the limitations of each method and the resulting limitations of the material collected.
- In order to provide a general overview, we triangulated the results of the different studies. This enabled us to get a global picture of HT in some countries and identify the critical areas that are already evident in the implementation of homogeneous research and safety data, in the shared standards for providing treatments and in regulation that is also based on common reference points. The last element is essential for consumer protection in general and, more specifically, when users might migrate to different countries<sup>2</sup>. In any case, even with the limitations that will be better explained later on, this study remains the first comprehensive study that seeks to take stock of HT at a global level.

## LIMITATIONS

Despite the range of methods used, this study has several limitations, with the most important listed hereafter.

- In terms of the scientific literature, mainly reviews were examined. Hence, this work might not cover the findings from more recent primary studies. The scientific quality of the material examined was

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<sup>2</sup> WHO, *Guidelines on Developing Consumer Information on Proper Use of Traditional, Complementary and Alternative Medicine*, WHO Geneva, 2004, available online at: <http://apps.who.int/medicinedocs/en/d/Js5525e/> visited on 14 May 2013

judged based on the commonly accepted parameter of the impact factor. On this basis, the quality of the reviews examined was variable, as well as the quality of the studies cited in the reviews. Moreover, very little material on safety was found. Given the focus on systematic reviews, the literature study is biased towards subjects or studies for which systematic reviews were published. Therefore, there is a publication bias. More, we found several studies that were publicized in “grey” literature that is not admitted into the main scientific magazines usually selected by the Medline database.

- The sociological part is exploratory. The user survey focused on a small purposive sample of regular users that is insufficient to show definitively the value of the therapy and, hence, it is not representative of the entire user group and, thus, not representative of the entire population.
- The findings could nevertheless shed light on how HT is perceived by the population and can be a model for further and more in-depth epidemiological studies.
- Likewise, the pool of experts who agreed to be interviewed and collaborated on this project may not be representative of all HT experts.

## WHO ARE THE PARTECIPANTS?

- **China:** Cao Wen Fu
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- Igor Bobrovinski
- **Tunisia:** Taoufik Khalfallah.

Each expert identified the HT centres to be sent a multiple choice questionnaire. The figures and tables that are shown in the relevant chapter contain only the most statistically significant data calculated using the monitoring survey questionnaire.

## DEFINITION

HT is the use of the water in different physical conditions and chemical compositions with many methodologies - both traditional and scientific - to treat and prevent health problems as well as to keep people healthy.

HT can be classified under the label of traditional medicine (TRM) as clearly specified in WHO's "General Guidelines for Methodologies on Research and Evaluation of Traditional Medicine", Geneva WHO/EDM/TRM/2000.1, pg. 9<sup>3</sup>.

Anyway, in some countries it is classified under the label of complementary and alternative medicines (CAM)<sup>45</sup>.

Europe has no clear tradition of TRM, meaning that HT, given its history goes right back to the Romans, should be seen as Europe's traditional medicine.

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<sup>3</sup> In WHO, *General Guidelines for Methodologies on Research and Evaluation of Traditional Medicine*, available online at: [http://whqlibdoc.who.int/hq/2000/WHO\\_EDM\\_TRM\\_2000.1.pdf](http://whqlibdoc.who.int/hq/2000/WHO_EDM_TRM_2000.1.pdf), visited on 14 may 2013

"2.1 Types of traditional procedure-based therapies

Traditional procedure-based therapies are therapies that use various techniques, primarily without the use of medication, to provide healthcare. They include, for example, acupuncture and related techniques, chiropractic, osteopathic and manual therapies, qi-gong, tai ji, yoga, naturopathy, thermal medicine, and other physical, mental, spiritual and mind-body therapies.

<sup>4</sup> In 2007 the National Center for Complementary and Alternative Medicine (NCCAM) of the National Institute of Health (US) defined these medicines as a "group of diverse medical and healthcare systems, practices and products that are not currently considered to be part of conventional medicine". These therapies are referred to as 'complementary' when they are used jointly with conventional treatments, and as 'alternative' when they are used instead of conventional treatments.

<sup>5</sup> Int. J. Biometeorol 2010 Sept; 54(5): 495-507 A proposal for a worldwide definition of health resort medicine, balneology, medical hydrology and climatology.

## INTRODUCTION

Despite being one of the oldest known treatments, HT has received very little attention from the scientific community, especially in recent years. Most of the information presented here is taken from old papers documenting the ancient and traditional use of this medicine through out the world. Anyway some recent studies that focus on the clinical effects and patient responses have also been included.

## HISTORY

### The origins

HT's original function in human history was as a cleansing and purifying element, often linked to specific religious rituals in the Mediterranean basin, the areas influenced by Jewish<sup>6</sup> and Minoan civilizations.

On the other hand, it is important to remember that HT is one of the most ancient and widespread treatments, used by numerous different peoples, including the Egyptians, Assyrians, Persians, Greeks, Jews, Hindus and Chinese. In many cultures and civilizations, human beings, especially if sick or dying, used fountains, basins and pools to benefit from the regenerating and curative power of water. The most ancient civilizations used water to purify the earthly body and cleanse the spirit from spiritual sins, in the belief that a clean and pure body would help the soul renew itself.

The main historical mentions of HT, during the pre-Hellenic period, come to us from the classics, such as the *Iliad* and the *Odyssey*. Bathing or swimming in the sea to regenerate a tired body was one of the most common uses of water<sup>7</sup>, along with purifying baths as a token of respect both for the guest and the landlord<sup>8</sup>, baths for daily cleaning<sup>9</sup> or washing after some labour-intensive task<sup>10</sup>. Purifying baths were also taken before making a sacrifice to the gods<sup>11</sup>.

There is no record of public baths in Athens before the 5th century BC. Hot baths were seen as a sign of slackness and a corruption of customs, explaining why Athenian laws banned the construction of bath houses inside the city walls.

It was only later that they developed to become places for meeting, socializing and learning (as they offered the opportunity to listen to philosophers and poets).<sup>12</sup>

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<sup>6</sup>*Le Sanctuaire de Sainte Anne et la Piscine Probatique de Jerusalem*, H. Vincent; *Kings*, IV 5-12; *Hygiene Die der Juden*, Gruenwald, 1911; *Talmud Siad.*, 25

<sup>7</sup>*Iliad*, X, 572-578; *Heroicus*, Philostratus, 3, 35

<sup>8</sup>*Odyssey*, VII, 457; XVII, 90

<sup>9</sup>*Odyssey*, VIII, 248-249

<sup>10</sup>*Odyssey*, X, 364; *Iliad*, XXII, 442-444; X, 572-578

<sup>11</sup>*Odyssey*, IV, 750-752; 759-761

<sup>12</sup>*Dict. Des antiq. Grecques et Romains* s.v. Balneum, see Daremberg and Saglio

The admission fee to the baths was not high, so everyone could afford them.

## The Classic World

The first examples of medical literature in which medical hydrology is mentioned are those contained in the *Corpus Hippocraticum*. Hippocrates was the first to deal systematically with the topic of water, its use, its effects on the human body and its correlation with disease.<sup>13</sup>

In numerous ages, water from differing sources and of varying types used to be channelled to temples. Lots of water, for instance, used to flow to Sanctuary of Asclepius. It was channelled using special piping, influencing the treatment provided back in those days.<sup>14</sup>

Despite the lack of direct testimony, the Etruscans too can be considered to be devoted to water, given the wealth of springs in their land, as documented by the Etruscan artefacts that have been found<sup>15</sup>. These artefacts show the high regard in which this ancient people held water. All the findings show that the Etruscans and the neighbouring populations were experts in using water to preserve health and treat disease.

Given how common water was in Rome, it is rational to conclude that Rome is the mother for all spa treatments. Spas were very common in Rome and throughout its huge empire, where a number of treatment centres thrived and grew.<sup>16</sup>

It is important to recall that the true use of HT as a medical therapy started in Rome with Asclepiades of Bithynia, a famous physician, who arrived in the capital in the 1st century BC as a rector. However, he was so successful as a physician that soon he gained the trust of leading Roman families. Indeed, before Asclepiades, Romans were wary of using HT. Water was generally only used for cleansing, with water treatments being a rarity.<sup>17</sup>

Genuine HT, based on the physical properties of water and especially its temperature, was based on the concepts from the methodical school of medicine. This drew from the atom theories of Democritus of Abdera, later taken up by Epicurus and implemented by Asclepiades, and saw being healthy and sick in terms of a harmonic relationship between pores and atoms. Specifically, *status strictus* was characterized by congestion, heat, agitation, and nervousness. For such an imbalance, warm baths and fomentations to help the pores dilate were the recommended treatments. By contrast, *status laxus* was characterized by pallor, exhaustion, abundant perspiration and muscle hypertonia. It was thought best to treat

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<sup>13</sup>*De usu humidorum*, chap. I; *Ibid*, chap. II, III; *De victus ratione in morbis acuti*

<sup>14</sup>Antigonus of Carystus, 3rd cent. BC

<sup>15</sup>*Trattato di Idroclimatologia*, Messini, p. 41

<sup>16</sup>*Aeneid*, Virgil, VII, 81 and following; Strabo, V, 3, 11; Pausanias, IV, 35; *Naturalis historia*, Pliny, XXI, 2; *The Twelve Caesars: Book II Augustus*, Svetonius, 82

<sup>17</sup>*De Re Medica*, Celsus, II-XVII; *Naturalis Historia*, Plinius, XXVI, 3

this with cold baths and showers to deal with the excessive relaxation of the pores.<sup>18</sup>

Celsus, in his famous work *De Medicina Libri Octo*, is a strident supporter of HT. He looks at the bath from all angles, as a means to treat, clean, and relax after physical exertion. In his work, he describes how bathing is an essential part of personal hygiene. He also recommends water for drinking or very diluted natural drinks that can support and accompany the therapeutic action of the bath, favouring diuresis to clear "bad humours".<sup>19</sup>

In the thirty-first book of *Naturalis Historia*, Pliny provides an exhaustive treatise on hydrology. Water is examined in terms of its role in therapies, hygiene, hydraulics and, more generally, its "wonderful effects".<sup>20</sup>

This short historical overview would not be complete without mentioning Galen. This great physician studied this topic extensively, looking at it in the light of it being a treatment using spa or plain water and also as a form of balneotherapy. To explain how HT worked, Galen largely used the statements from the methodical school.<sup>21</sup>

The abundance of water in Roman lands led them to favour bathing from early in their history, often bathing directly in the Tiber or in both manmade and natural pools. It was only later, probably in response to local water source becoming more scarce, that Romans started to channel water to Rome from further afield.<sup>22</sup>

Neighbouring areas were also enriched with large spa houses, explaining why, for example, one of our best remaining examples of an ancient spa is the Terme Stabiane (Pompeii), built around the 2nd century BC<sup>23</sup>. In Rome, one of the most striking spa baths built after the fire of Rome (64 AD) were the Agrippa<sup>24</sup> and Nero spas. However, the most famous spas from Imperial Rome were the Caracalla (opened in 217) and Diocletian ones (built between 298 and 306).

In the Imperial Age, the spas were a meeting point, a place to gossip, plot, see and be seen, but also a place of culture, physical exercise and art<sup>25</sup>. The essential rooms, according to Vitruvian rules, were the *laconicum*, *calidarium*, *tepidarium* and *frigidarium*. The first room would be very hot, heated via niches, and the patient would crouch and have a sweat bath. The *calidarium* was a room with a hot pool on one side. Opposite the pool, there was a *labrum*, where in a large fountain water would overflow so the patient could have a sort of cold shower. The next step

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<sup>18</sup>*Vero metodo di servirsi dell'acqua fredda nelle febbri e in altri mali, sia interni che esterni*, Nicolò Lanzani, Naples, 1719; *Il passato e l'avvenire dell'idrologia medica in Italia*, L. Chiminelli, Florence, 1885

<sup>19</sup>*De Re Medica*, Celsus, I, 1; *Ibid.*, Celsus, III, 6; op. cit. Celso, I, 3-4-5-10; III, 9-14-22; IV, 1-5-17; V, 28; VI, 12

<sup>20</sup>*Naturalis Historia*, Pliny, XXXI 2;

<sup>21</sup>*De methodus medendi*, Galeno, I, X, p. 65 h; *De sanitate tuenda*, Galeno, III-IV

<sup>22</sup>*Notizie sulle origini ed approvvigionamento idrico*, Druetti, vol. II, part I, 1939

<sup>23</sup>See *Dedication writing*, in "Corp. Iscr. Lat", X, 829

<sup>24</sup>*Documents inédits sur les Thermes d'Agrippa*, Geymuller, Lausannes, 1883;

<sup>25</sup>*Epistle*, Seneca, 56, 1, 2; *L'idroterapia ai tempi dell'impero Romano*, Di Capua, Rome, 1940; The Pedagogus, Clement of Alexandria, III, 9

was the *laconicum*<sup>26</sup> for the sweat bath<sup>27</sup>. After the sweating stage came the *tepidarium*, where the temperature was lukewarm. Finally, it was time for the *frigidarium*, with a large swimming pool filled with cold water. In some cases, there were also the *aliptherion*, a room for massages with oils and ointments<sup>28</sup>; and the *heliocaminus*, where people could sunbathe in a heated room.<sup>29</sup>

## The early Middle Ages

With the fall of the Classical world, the baths quickly declined, both in cities with large bath houses and in the spa resorts that had supplied the water for treating various diseases.

Wars, barbaric invasions and the hardship of that period led to the ancient aqueducts and spas falling into ruin, with the consequent abandonment of the baths.<sup>30</sup>

Some attribute this fall of hydrology not only to material decay, but also to a negative culture supposedly linked to Christian puritanism. However, despite these rumours, Christianity was never against the use of baths<sup>31</sup>, provided they were taken in a way that did not offend morality and did not trespass into promiscuity<sup>32</sup>. This specification is very interesting as it gives us an idea of what might have been happening in the public baths at the end of the Empire. During the Christian period, baths could be divided into two categories: those used for liturgical reasons and those with hygienic purposes.<sup>33</sup>

In certain respects, it was King Theodoric who took Rome's greatness forward and he devoted a large part of his rule to maintaining, restoring and improving the best aspects of Roman civilization<sup>34</sup>. Therefore, the Goths continued the long-standing hydrological tradition started by the Romans. However, Charlemagne was the one who placed the most importance on hydrology, although this was for historical rather than medical reasons. His desire to enjoy the benefits of the spas led him to

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<sup>26</sup>*Trattato teorico e pratico di balneoterapia e di idrologia medica*, Schivardi, Milan, 1875

<sup>27</sup>*Epistle*, Seneca, 86, 10; Petronius c. 72 *Epistle*, Pliny, III, 14, 2

<sup>28</sup>*Epistle*, Seneca, 56, 1-2;

<sup>29</sup>*De Architectura*, Vitruvius

<sup>30</sup>*Il museo epigrafico Pio Lateranense*, De Rossi, Rome, 1877, sec. III, an. II, 14 and following; *De bello Vandalico*, 1, Procopius, I; *Bellum Gothicum*, I, Procopius

<sup>31</sup>*I Santi nella storia della medicina; La medicina nel Monastero Bianco*, Pazzini p. 75, Rome, 1928; *Il monachismo prima di San Benedetto*, Albers, Rome, 1916

<sup>32</sup>*Il museo epigrafico Pio Lateranense*, De Rossi, sez. III, a. II, p. 14 and following, Rome, 1877

<sup>33</sup>*Conquiste idrologiche nei campi Flegrei ed in altre zone d'Italia dall'avvento del Cristianesimo e le Terme "Subveni Homini" a Pozzuoli*, in "Atti del IX Congresso Nazionale nei campi Flegrei", p. 79 and following, Naples, 1928; *De sacri christianorum balneis*, Paciandi, Rome, 1757; *Analecta Romana*, Grisar, pp. 101 and following.; *Liber Pontificalis*, Pope Adrian I, Duscense ed., p. 503

<sup>34</sup>*Geschichte Roms und der Papste in Mittelalter*, Grisar, I, p. 467; *Variae*, Cassiodoro, Ep. 39; *Trattato di Crenoterapia introduzione*, Benedicenti, p. 10

make the spas built in Aachen by Granus, Nero's brother, his royal palace.<sup>35</sup>

During the middle ages in Europe, curative pools were built using the thermal springs of Baden-Baden in Germany, Bath in England and Spa in Belgium. In a small village located in the Ardennes, some warm mineral springs were discovered to have medical and therapeutic properties. Spa was the word used to identify these. In terms of etymology, the word "spa" comes from the Latin: *salus per aquam* or *sanitas per aquam*, or *per aquas*, which literally means health through water.

The "acronym" was most commonly used, from which also the use in capital letters, namely SPA. In English "spa" refers to a resort or in general, company whose business is wellbeing, relaxation and care for the body. In truth, this is a case of false etymology, produced by the need to clearly make a difference from the Belgian trade name Spa, that originated in the spas of the city bearing the same name.

The truth is that the expression *salus per aquam* is not used by Latin authors and this expression just seems to be an acronym.

Already common in the English language, it refers to a source.

## The Renaissance

The 15th century saw renewed interest in man and his shape, leading to spas gaining ground once more as places to care for oneself. This led to a revival of this Classical tradition across the Western World. Medical treatise about the benefits of each individual source became increasingly common. Among these, it is worth mentioning the writings from the *Excerptade Balneis* collection, published by Giunti in 1553, and Bacci's *De Thermis*. During this period, some new spas were discovered, while others were revamped following the neglect of the Middle Ages.

HT in the Middle Ages and the Renaissance was based on a strictly naturalistic vision. Treatments were deemed useful for almost all diseases, with an aetiopathogenesis linked to humours. As such, the action of mineral water was seen as useful for re-balancing humours and eliminating altered or "sinful" humours<sup>36</sup>. It is worth highlighting that, while early ideas equated the action of water to magic, in the Middle-Ages and Renaissance a more strictly medical approach to HT was adopted. In this period, medieval and Renaissance writers created a clear separation between supernatural treatments and medical-pharmacological therapies, with HT in the latter category.

## Hydrology in the 17th and 18th centuries

As noted, the *galenic* concept of mineral water working to balance the humours saw water as being able to excite, modify or slow down the humours. This view was gradually replaced by the chemical-pharmacological concept, which focused on the activity of a given active ingredient. In ancient times the action of mineral salts was thought to

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<sup>35</sup>*Vita et gesta Karoli Magni*, Einhart

<sup>36</sup>*Trattato di Crenoterapia*, Benedicenti, p. 42



balance the humours, but later the actual mineral substances were considered as pharmacologically active.

More specifically, advances in the chemical analysis of mineral water and the desire to attribute to chemical reactions to most of the vital phenomena drove a surge in crenotherapy studies, which was increasingly considered to have a chemical basis.

Iatrochemistry (from the Greek *iatros* and *chemeía* chemistry) was a branch of chemistry and medicine that developed starting from the 16th century, at the same time as iatromechanics, whose leading light was the Swiss physician Paracelsus.

The basic idea of iatrochemistry lies in the belief that the health of our body mainly depends on the specific balance of the chemical elements contained in the bodily fluids. Based on this idea, the iatrochemists studied and interpreted biological processes (for instance fermentation) from a strictly chemical point of view. The human body, according to this view, is like a chemical furnace, where life is but a host of chemical processes to be explained and related to disease and its treatment<sup>37</sup>.

Starting from this concept, mineral water was reinterpreted as drugs that exerted their action on the body's fermentation processes, the concentration of salts and blood acidity.

In the 17th century, with the discovery of the New World, the English, Dutch and French colonialists built their houses in stone and placed wooden tanks next to the curative water of the local populations. The latter used steam baths and waterfalls both for therapeutic and religious purposes.

Thanks to contributions from the cultures of the new world, the spa tradition was reinvigorated. With John Wesley, founder of Methodism, it became one of the most popular ways for treating people.

In that period, many authors noted down their observations on the effects on the body of hot and cold water, coming to the conclusion that reducing heat could somehow benefit the nervous system.

### **Hydrology in the 19th and 20th centuries**

In these centuries, many treatises on hydrology, HT and crenotherapy were drafted. Tests were improved and so was the research designed to establish the chemical composition of the different types of water.

So, hydrology left behind the empiricism on which it based basically all of its practice and started to be interpreted through the observation of vital phenomena. According to the authors, HT, "attracting and regulating the production of heat, has a major influence on all bodily functions: it achieves the rapid decomposition and reconstruction of the tissues and a quicker and more complete regeneration of organic matter"<sup>38</sup>. In general, the main interpretations of how HT works are based on the fact that all

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<sup>37</sup> Van Helmont ; De La Boe

<sup>38</sup> *Trattato teorico-partico di balnoterapia e di idrologia medica*, Schivardi, Milan, p. 293

bodily activity increases during depuration and assimilation, exerting a positive influence on the entire body.

At the end of the 19th century, thermalism and HT spread throughout Europe with the development of spa centres such as Aix-les-Bains, Évian-les-Bains, Vichy, Baden-Baden, Montecatini, Abano, San Pellegrino, Karlsbad, Marienbad and Franzbad.

This was the period when Vincent Pressnitz did his work<sup>39</sup>. He was a farmer from Silesia, which created a centre for the use of cold water and physical exercise, allowing him to conduct research on tissue response to different temperatures and its reaction to diseases. Soon enough, this centre became a place with external baths where patients would follow treatment programmes involving cold showers and massages.

However, it was Father Sebastian Kneipp (1821-1897) who brought HT to the broader public. He changed the Pressnitz treatment technique, alternating applications of cold showers with hot baths, even selectively on parts of the body. This form of HT, known as "Kneipp medicine", became extremely popular in France, Italy and the Netherlands. Even today, it remains very common.

HT gained ground everywhere. In the UK, around 1840, HT started to be considered a marginal technique, although it was widely used in hospitals, nursing homes and wellbeing centres.

In 1900, HT was more successful in the US, where it was commonly practiced in spa centres.

During the world wars - especially the second - the need to use water for exercise and to maintain fitness was stressed. This paved the way for the current use of swimming pools and immersions in HT rehabilitation treatment for a wide array of diseases.

In 1950, American physiotherapists started to be trained about physical treatments in water and the relevant indications. The excellent results obtained with therapies in water received positive feedback from many orthopaedic surgeons, helping this method to spread across the world.

## **HYDROTHERAPY**

HT is the use of the water in different physical conditions and chemical compositions with many methodologies - both traditional and scientific - to treat and prevent health problems as well as to keep people healthy.

In the light of the developments in HT, it would be appropriate to divide it into a part that essentially makes use of the physical properties of water and a part - more specifically called crenotherapy or sometimes balneotherapy - that, in addition to the physical properties, also uses specific chemical properties of mineral water

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<sup>39</sup>*Trattato tecnico pratico di balneoterapia e di idrologia medica*, Schivardi, Milan, p. 290

HT, strictly speaking, exploits the characteristics of water such as buoyancy, temperature and pressure, regardless of any pharmacological properties linked to mineral salts.

## PHYSICAL PROPERTIES OF WATER

Water has some unique properties that determine its efficacy as a therapeutic medium. One of the most important being its capacity to retain and give back heat. Indeed, comparing this capacity to that of other fluids, water - given the same weight - is able to absorb more heat than any other substance, almost twice as much as alcohol or paraffin, 10 times more than copper or iron and 30 times more than lead or gold. In addition, water is a good conductor of heat. Thanks to its intrinsic characteristics it has the capacity to easily change temperature.

The maximum and minimum temperatures for the use of water vary between 0-5 and 45-100°C. In general they are divided as follows:  
extreme temperatures: 0-5°C. In this case, water is used as ice for local cryotherapy compresses;

- very cold: 5-11°C;
- cold: 12-16°C;
- nearly cold: 17-27°C;
- neutral: 28-36°C;
- warm: 37-38°C;
- very hot: 39-45°C;
- at extreme temperatures: 45-100°C.
- temperatures for steam baths <sup>40</sup>.

This classification is related to the stimulation of the peripheral nerves and varies depending on water temperature, the duration of the application, and the method of application.

Generally considered as a universal solvent, water can easily be used as either a systemic or topic therapy.

In the liquid state, water can be applied as hot or cold packs, baths, sprays, and showers at any temperature and pressure. In the form of vapour, it can be used as a steam bath or for inhalation.

Furthermore, since the density of water is close to that of the human body, it can be used as a method of exercising in rehab programmes involving hydro and kinesitherapy. In addition, hydrostatic pressure on the body surface, following immersion, improves venous and lymphatic return as well as the function of the excretory organs.

Using water offers a universally available and easily accessible possible therapy that requires relatively simple and inexpensive equipment.

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<sup>40</sup>*Trattato di idroclimatologia clinica I*, Messini, p. 581-582

## **Primary actions**

Physiologically, HT works both through thermal and mechanical actions. The thermal action is achieved by applying water at a temperature higher or lower than that of the human body. The higher the variation from body temperature, the greater the effect, even without changing any other factor. The mechanical action is produced by the impact of the water on the body surface (such as spray, shower, hydromassage, rubbing etc.). The most often used action in HT is thermal. Heat can be transferred from one object to another in many different ways. In HT, heating and cooling is produced by the transfer of heat from the water to the body. The body comes in contact with the water by means of baths, showers, sprays, packs, compresses and so on. When talking about water temperature, we use the words "hot" and "cold" to refer to body temperature. The range of temperatures that are useful for HT varies from very cold to very hot.

Thus, the variation in body temperature can be seen as a significant factor in HT.

## **Secondary action of cold application**

Cold application can be done by using ice, cold water and air or, alternatively, using the evaporation of water or other fluids from the body surface.

The primary effect of cold application in nature is that of slowing down general functions, both at a local and systemic level.

The depressive action is more powerful the longer the duration of the application and the lower the temperature. However, under normal conditions, the body responds to a lower temperature through a secondary activation known as a "reaction". Obviously, this reaction takes place provided the body has adequate capacity to respond to the cold.

## **Secondary action of hot application**

Hot applications cause an increase in perspiration, and breathing and heart rate as the body seeks to combat the increases in local and systemic temperature.

Water at 36.6°C or higher is perceived as hot. At 40°C it is perceived as boiling. At 48.8°C, bathing is unbearable. The mucous membranes, unlike the skin, may endure temperatures up to 57.2°C, which accounts for our ability to drink very hot liquids. Hot air can be tolerated for relatively long periods of time, as happens with saunas, where the temperature can go up to 110°C.

## **Principles of blood circulation and hydrotherapy**

If it is true that to promote healing, either locally or systemically, it is important to maximize oxygen circulation and remove any waste products, then HT techniques are one of the most effective means of accomplishing this.

In order to achieve these changes, many effects of HT on blood circulation have traditionally been described as being able to facilitate healing. The main ones include:

- revulsive effect;
- derivative effect;
- spinal reflex;
- arterial trunk reflex.

### **Revulsive effect**

The revulsive effect provides a means to increase the rate of blood flow through an organ or an area of the body, such as a limb. It is most effectively accomplished by alternating hot and cold in the form of baths, showers, sprays, etc.

It is commonly held that local contrast applications, hot and cold, produce marked stimulation of local circulation.

Given the increase in blood flow in a specific area of the body, the revulsive effect is ideal for treating situations presenting primarily as congestion. An example of this is using alternating hot/cold compresses over the face for sinus congestion. As a powerful decongestant, the revulsive effect also acts as an analgesic for the pain resulting from congestion.

### **Derivative effect**

The derivative effect can be seen as the opposite of the revulsive effect. Its main purpose is to change blood volumes by shifting blood from one area/organ of the body to another. For example, prolonged application of heat to the feet, as with a hot foot bath, decreases congestion in the head. This form of treatment can be very effective for certain forms of congestion headaches. As a general rule, the wider the body surface exposed to the application, the greater the effect.

### **Spinal Reflex**

The spinal reflex effect provides a means of affecting a distant area of the body through a local application. Indeed, a sufficiently intense local application of heat or cold not only affects the immediate skin area, but also causes remote physiologic changes, mediated through spinal reflex arcs. These effects have been carefully observed over many years and

have led to a mapping that correlates each surface area with a corresponding internal area and/or an organ.

### **Arterial Trunk Reflex**

The arterial trunk reflex effect is a special case of the general reflex effect. It has been observed that a prolonged cold application over the trunk of an artery produces contraction of the artery and its distal branches. Prolonged hot applications have the opposite effect, producing dilation in the distal arterial bed.

For example, prolonged hot applications over the femoral artery in the groin can be used to increase circulation in the foot or the ankle, which is limited due to arterial spasms.

## **HYDROTHERAPY TECHNIQUES**

The ways in which water may be applied to the human body are generally simple and inexpensive. In the past, a number of techniques have been uncovered for applying water and many are still used today. The following provides a short list of the main ones.

### **BATHS**

Bath water may simply contain spring water or additional substances such as herbs, medication and mineral salts that dissolve in the spa bath. In addition, they may be in an agitated state, as with a whirlpool or hydromassage bath.

#### **Hot baths, with full immersion**

Hot baths are given within a temperature range between 37.7-41.1°C, for as long as 20 minutes. They are indicated for the treatment of musculoskeletal pain, to aid in relieving muscular spasms, for cleansing the body and to induce sweating.

In most instances, hot immersions are best followed by a brief cool bath, shower or spray. Prolonged hot tub baths are never appropriate for the very old or very young, weak or anaemic people, individuals with organic diseases, or in anyone with a tendency to haemorrhage.

#### **Neutral baths**

The neutral bath is a full immersion bath given at an average temperature between 33.3-35°C. The patients should have neither the sensation of being warmed, nor that of being cooled. Since the ideal temperature depends on the patient's condition and reaction to the water, it is often best to use his/her sensation, rather than a thermometer, as a guide to adjusting the temperature. The duration of a neutral bath may vary from 15 minutes to 4 hours.

The primary effect of a neutral bath is sedative, with a calming effect on the nervous system. A second effect is the activation of the kidneys and increased urinary output, due to the absorption of water into the body during prolonged immersion.

Lastly, a neutral bath causes a decrease in the surface temperature of the body, due to the lack of the usual heat (produced by the skin.) When prescribed for home treatment, a neutral bath is best taken just before getting into bed to avoid cooling. Traditionally, neutral baths are prescribed in cases of insomnia, pain, anxiety, nervous irritability and chronic fatigue.

### **Cold Baths**

Cold baths must be taken in an environment with a pleasant temperature, with a water temperature between 15 and 18°C. They can be repeated, but this will depend on personal endurance. Before taking a cold bath, it would be best to do a bit of physical exercise to warm up, or alternatively use rubbing (friction) or a hot foot bath. After the bath, the patient will need to go to bed to be warm and favour a hyperaemic response. It can be followed by a cold sponge bath.

Appropriate herbs, salts or other drugs may be added to the water to optimize the treatment.<sup>41</sup>

### **SHOWERS**

A rainfall shower consists of a shower head that, like a watering can, can have more or less holes, depending on whether one wishes more or less, bigger or smaller drops.

The column shower consists of a single solid jet of water.

Any cold shower should be quick and use a pressure of no less than one atmosphere and no more than three. Mixed showers, between 22 and 34°C, may last from 2 to 4 minutes, if at low pressure. Scottish showers involve increasing the temperature from 26 to 40°C and then gradually going down to 10°C. A hot shower is given at a temperature between 38 and 44°C, for a time between 1 to 3 minutes, proportional to the maximum planned temperature.

Showers are re-invigorating and energizing, both for their thermal and mechanical action. Showers normally increase strength, tactile and pain sensitivity and have an influence on blood pressure. Organic exchange is more active and energetic with showers. As regards indications, rainfall showers are especially good for patients with arthrosis. Jet showers are best for patients with neuropathies, low blood pressures and amyotrophy. Under water showers are used for sciatica. Showers used for the locomotor system are generally hot, however, in some instances (gout, sciatica etc.), it is more beneficial to have contrast or Scottish showers.<sup>42</sup>

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<sup>41</sup>*Trattato di idroclimatologia clinica*, Messini, p. 582-585

<sup>42</sup>*Manuale di Medicina Termale*, Agostini, p. 51; *Medicina Termale*, Solimene, Bruttomesso, p. 71-74; *Trattato di idroclimatologia clinica I*, Messini, p. 587-589

## **COMPRESSES**

Compresses come in three basic types: hot, cold and alternating hot and cold. They are each applied using cloth or another compress material, which is wrung out to the desired degree of dampness and then applied to any surface of the body.

### **Cold Compresses**

A cold compress is a cold or frozen cloth that is applied to the body. Solutes may be added to the water, such as salts, sodium bicarbonate, Epsom salts, boric acid or cider vinegar. Some herbs may also be added for a more specific effect.

The cold pack or compress has primarily a vasoconstrictive effect, both locally and distally. Due to this effect, it may be used to prevent or relieve blood flow to an area, stop bruising after injury, inhibit inflammation and relieve pain. It may also be used to reduce body temperature, when applied over a large area of the body.

Cold compresses are renewed frequently (every 1-5 minutes) to maintain the primary cold effect. The temperature of a cold compress depends on the specific problem being treated, as well as the patient's health.

### **Hot compresses**

Hot compresses are prolonged applications of moist heat to a local area of the body. They create a derivative effect which increases blood flow to the periphery, thus decreasing internal congestion. This technique may be used to increase blood flow to an organ, to stimulate certain organ functions and to produce tissue warming and relaxation. Hot compresses may be beneficial for their sedative effects in treating insomnia, nervous tension and mild muscular spasms.<sup>43</sup>

## **COLD FRICTION RUBS AND ABLUTIONS**

Cold friction rubs, or ablutions, consist of rubbing the body in a predetermined sequence with cold water. They are done with rough materials, such as a coarse washcloth or a loofah.

Ablutions are carried out with the patient lying supine. Depending on the desired cooling effect, the mitt may either be saturated or wrung dry.

The main effect of a cold ablution is toning.<sup>44</sup>

## **GENERAL GUIDELINES FOR HYDROTHERAPY**

The first rule for HT is the same as for any therapy: treat the whole person. This involves considering medical history, current condition,

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<sup>43</sup>*Trattato di idroclimatologia clinica I*, Messini, p. 585-586

<sup>44</sup>*Trattato di idroclimatologia clinica I*, Messini, p. 586



current medications and any other relevant information. After acquiring a holistic view of the patient:

- use HT treatments in a coordinated and integrated manner with any pharmacological treatments the individual is receiving;
- use HT treatments in a manner that is suitable for the general and specific health of the patient;
- explain the procedure before the start, including the technique used (duration, frequency and any other relevant factors), making sure the patient feels comfortable during treatment;
- check the patient's body temperature before starting a treatment. If the temperature is lower than normal, it is possible to use more heat or prolong the application of heat. If the body temperature is higher than normal, use less heat and make the cold application longer during treatment.

Over time the range of disorders and conditions indicated for thermal treatment has grown wider. This is partly related to how the concept of health is seen, especially since it is no longer viewed as the simple absence of a specific disease, but rather as a state of psychological and physical wellbeing.

In general, however, it is fundamental to carry out a preliminary medical assessment and be especially cautious with patients with diabetes, heart-disease, hypertension, kidney disease, severe liver disease, transplant patients or patients with pace-makers or any other medical device etc.

As a general principle, it is recommended to do treatments in the most suitable times of the day: before meals or at least 1 hour after meals. It might be very useful to take into account the circadian rhythm of the body.

## **HYDROTHERAPY TREATMENT INDICATIONS**

When starting a HT treatment, it must be noted that it takes effect at two different levels, curing the problem and providing symptom relief. For some conditions, HT treatment can provide the solution, while for others the main purpose is to provide symptom relief. However, there are cases in which this distinction is not that clear-cut, as in arthrosis. In this condition, it is possible to obtain functional improvement and slow the disease's progression. Many other diseases for which HT is prescribed fall under the category of chronic and/or degenerative diseases, for which there are no definitive cures.

However, often, HT is effective not only on symptoms, but also on the organic problem that lies at the root of the disease and its worsening. This

effects both the disease specifically and in general, for instance, by stimulating the immune system, reducing inflammation and modulating hormonal levels.<sup>45</sup>

In the current paper, under the paragraph "*Status of hydrotherapy evidence*" p. 43, some indications that have been validated in certified scientific studies have been reported. Without a doubt, though, many of the applications and indications for this method come from a heritage of traditional knowledge, practice and methods that date from many centuries ago. According to the indications contained in the WHO document<sup>46</sup>, however, it is clear that the challenge posed by the growth in these methods requires, especially for consumer protection, an increase in the level of research to support its safety, efficacy and correct use for various conditions, disorders and diseases.

## HYDROTHERAPY WITH MINERAL WATER

Therapy with mineral water is referred to as "Crenotherapy" (from the Greek Krene, i.e. "source"). There are basically two types of crenotherapy: internal and external<sup>47 48 49</sup>.

Internal crenotherapy includes hydropinotherapy (or drinking thermal water), irrigations (vaginal, nasal, oral, intestinal or rectal) and inhalations.

External crenotherapy includes balneotherapy (i.e. treating some disease with immersion baths, hydromassage, showers, mineral water injections etc.) and peloid (mud) therapy.<sup>50</sup> Some consider psammotherapy (sand bathing), hydrokinesitherapy and speleotherapy (exposure to mineral salts in thermal caves) as part of crenotherapy.<sup>51</sup>

The term mineral refers to bacteriologically pure water that originates from an underground water table and/or comes from a spring that wells up in one or more natural or artificial sources. Water is deemed to be more or less mineralized, depending on the quantity of minerals it contains. The first studies to classify mineral waters date to 1670, when the Academy of Science in France developed testing methods that are still used today<sup>52</sup>.

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<sup>45</sup> *Medicina termale*, Solimene, Bruttomesso, p. 118-119; *Trattato di idroclimatologia clinica I*, Messini, p. 600-602

<sup>46</sup> WHO, *WHO-TRM Strategy 2002-2005*, WHO Geneva, 2002, available on line at: <http://apps.who.int/medicinedocs/en/d/Js2297e/> visited on 14 May 2013

<sup>47</sup> *Medicine thermal*, P. Queneau, M. Boulangé, A. Françon, B. Graber-Duvernay, C. Laroche, J. Oudot, C. Roques, Masson, p. 39

<sup>48</sup> *Medicina Termale*, Solimene, Bruttomesso, p. 13

<sup>49</sup> *Medicine thermal*, P. Queneau, M. Boulangé, A. Françon, B. Graber-Duvernay, C. Laroche, J. Oudot, C. Roques, Masson, p. 25

<sup>50</sup> *Manuale di Medicina Termale*, Agostini, p. 39;

<sup>51</sup> *Medicine thermal*, P. Queneau, M. Boulangé, A. Françon, B. Graber-Duvernay, C. Laroche, J. Oudot, C. Roques, Masson, p. 80

<sup>52</sup> *Medicina Termale*, Solimene, Bruttomesso, p. 17

For national classifications, please refer to the ones used in each country. For further info, visit: <http://femteconline.org/>.

## **CHEMICAL AND MINERAL CHARACTERISTICS OF THERMAL WATER**

Water is one of the most common compounds found in nature. Inside biological structures, water molecules can either be free or bonded with some other element.

From a biological perspective, it is clear that with an increase in salt concentration, the quality and quantity of the dissolved electrolytes has a greater impact on the pharmacological effect. Water with a very low salt content is "thirsty for salts". It is rapidly absorbed and acquires sodium and catabolites that reach the kidneys and have a diuretic effect.<sup>53</sup>

Water with high ion content is hypertonic in relation to body fluids. So it is not absorbed and not "thirsty for salts", but rather attracted to the intestinal lumen, producing the need to empty the bowels. Therefore this is a laxative-purgative water, with the power of the effect related to salt concentration. Between these two extremes there is a range of mineral water that is used in classic hydrology treatment. Each type, in relation to its specific chemical and physical characteristics, is indicated in the treatment of specific conditions.<sup>54 55</sup>

### **Arsenical-ferruginous water**

These waters contain, in variable proportions and depending on the classification adopted in a given country, both arsenic in the form of arsenic or arsenate, and iron either as a ferrous or ferric ion, either separately or in combination. Pure arsenical water is very rare. This type of water is used for anaemia, hyperthyroidism and anxious neurosis or hyper-sensitivity. Such water is generally administered as a drink during meals. It is recommended for balneotherapy to treat "dry" skin problems (eczema, psoriasis, etc.).<sup>56</sup>

### **Waters with bicarbonate**

Anion bicarbonate ( $\text{HCO}_3^-$ ) is the predominant element or is at least present in significant quantities. The exact amounts are defined by the relevant regulations in each country. Such water has a "biphasic" effect and can be used both in hypochlorhydria and hyperchlorhydria induced gastritis. Most of the salts contained in the water are dissolved as calcium, magnesium, sodium, potassium bicarbonate etc. It can be drunk, and used for external (mud and baths) or internal crenotherapy (inhalations or irrigations). It has an evident diuretic effect. They boost

<sup>53</sup> *Vademecum of spanish mineral-medicinal waters*, Instituto de Salud Carlos III, p. 11

<sup>54</sup> *Manuale di Medicina Termale*, Agostini, p. 8-9;

<sup>55</sup> *Medicine thermal*, P. Queneau, M. Boulangé, A. Françon, B. Graber-Duvernay, C. Laroche, J. Oudot, C. Roques, Masson, p. 8

<sup>56</sup> *Manuale di Medicina Termale*, Agostini, p. 28; *Medicina Termale*, Solimene, Bruttomesso, p. 31-33

the action of the digestive enzymes produced by the pancreas by increasing secretion. They aid intestinal digestive processes. In special diets, such water is indicated for treating hypertension and osteoporosis. It is recommended for sports people and to wean babies.<sup>57 58</sup>

### **Carbonic water**

Such water springs up naturally containing free carbon dioxide (CO<sub>2</sub>). This type of water can be used for drinking, with the same indications as for water with bicarbonate and, above all, as the main treatment for vein conditions. Indeed, the action of carbonic water on peripheral blood flow is key. During the bath, the carbon dioxide causes intense hyperaemia, with vasodilation and a clear reduction in blood pressure, both diastolic and systolic.<sup>59</sup>

### **Water with sodium chloride**

These mineral waters contain a large quantity of the cation Na<sup>+</sup> and the anion Cl<sup>-</sup>. Depending on the prevalence of other anions and cations and the treatment action, such water can be further classified as follows: salt-sulphate, salt-sulphate-alkaline; salt-arsenical-ferruginous; salt-bicarbonate. Water with bicarbonates are generally drunk. It causes an increase in bile formation and in the flow into the duodenum. It is generally indicated for poor digestion caused by an insufficient production of gastric juices. Hypertonic water has a laxative effect.<sup>60</sup>

### **Radioactive water**

The term radioactive is used to describe water that, regardless of the other chemical-physical elements it contains, has large amounts of Radon. In thermal practice, in general Radon 222 is the element taken into account. Radon is four times more soluble in water than in the air. The easiest way for Radon to get into our body is by inhalation, followed by drinking and finally balneotherapy.<sup>61</sup>

It is very useful to treat chronic obstructive pulmonary disease, especially asthma. The efficacy seems to be linked to the direct action on the sympathetic nervous system, which is stimulated to cause bronchodilation. The liposolubility of Radon in the myelin sheath would account for most of its therapeutic effect. The depolarization of the nervous fibres slows down the speed of nerve impulses, with a general analgic effect. Traditionally, radioactive applications in crenotherapy have been recommended for pain in osteoarthritis, degenerative

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<sup>57</sup> *Manuale di Medicina Termale*, Agostini, p. 23; *Medicina Termale*, Solimene, Bruttomesso, p. 34-35

<sup>58</sup> *Vademecum of spanish mineral-medicinal waters*, Instituto de Salud Carlos III, p. 280

<sup>59</sup> *Manuale di Medicina Termale*, Agostini, p. 24-25; *Medicina Termale*, Solimene, Bruttomesso, p. 36-38

<sup>60</sup> *Manuale di Medicina Termale*, Agostini, p. 25-28;

<sup>61</sup> *Vademecum of spanish mineral-medicinal waters*, Instituto de Salud Carlos III, p. 282

arthropathies, ankylosing spondylitis and following trauma with severe pain.<sup>62</sup>

#### **Water with salt, bromine and iodine**

Such water is sea water with iodine and bromine. It is often used in very concentrated form according to Beaumé's scale<sup>63</sup>.

The stimulating metabolic effect, clearly separates this type of water from arsenical-ferruginous water, especially because of the presence of iodine. As per the tradition, such water is prescribed to lethargic people with a tendency to put on weight. This clearly contrasts with the previous type of water. The marked hypertonic nature of this water play a key role in the action mechanism. The anti-inflammatory action is clear, especially in forms with a poor tendency to heal. The action mechanism involves focal reactivation. The use of such water in treating vascular conditions is becoming increasingly important, especially with phlebitis.<sup>64</sup>

#### **Sulphate water**

This water contains mainly  $\text{SO}_4^-$  anions at values that are defined by regulations in each country. It is a purgative water. Sodium and magnesium sulphate, which are not easily absorbed, attract water to the bowel. There is also the direct action of the anion on the muscle fibre cells, causing the bowel to empty. The water has a mucolytic and anti-inflammatory effect on the mucous membranes.<sup>65 66</sup>

#### **Sulphurous water**

Sulphurous water is water with a high content in bivalent sulphur ( $\text{S}^{--}$ ). The multitude of chemical types of sulphur contained in mineral water, which are perfectly balanced, makes the pharmacology of such sources extremely complex. Due to the action on the parasympathetic nervous system, a sulphur mud or bath causes intense vasodilation, with a decrease in blood pressure. This makes sulphurous water especially good for treating vascular diseases, venous or post-traumatic ulcers and burns. The vagal stimulus also accounts for the laxative action of such water. Sulphurous water is also very useful for respiratory disorders, such as rhinopharyngitis, laryngitis and bronchitis. It is also beneficial for the skin, the digestive tract and rheumatism.<sup>67 68</sup>

### **THERMAL WATERS: INDICATIONS FOR TREATMENT**

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<sup>62</sup> *Manuale di Medicina Termale*, Agostini, p. 31-35; *Medicina Termale*, Solimene, Bruttomesso, p. 41-43

<sup>63</sup> Antoine Beaumé, a French chemist (1728-1804), invented this scale in 1768 (hence the name of the device). The device he invented was used to determine the specific weight of liquids that were less dense than water (it is for "spirits").

<sup>64</sup> *Manuale di Medicina Termale*, Agostini, p. 28-29; *Medicina Termale*, Solimene, Bruttomesso, p. 26-29

<sup>65</sup> *Manuale di Medicina Termale*, Agostini, p. 29; *Medicina Termale*, Solimene, Bruttomesso, p. 24-25

<sup>66</sup> *Vademecum of spanish mineral-medicinal waters*, Instituto de Salud Carlos III, p. 279

<sup>67</sup> *Manuale di Medicina Termale*, Agostini, pp. 29-31; *Medicina Termale*, Solimene, Bruttomesso, p. 20-23

<sup>68</sup> *Vademecum of spanish mineral-medicinal waters*, Instituto de Salud Carlos III, p. 281

The following table shows a list of the main types of thermal water used to treat different disorders or diseases.<sup>69 70</sup>

DISEASE	MAIN WATER USED
ENT and respiratory	Sulphurous Salt, bromine and iodine Bicarbonate Arsenical-ferruginous
Cardiovascular	Carbonic
Gynaecological	Sulphurous Salt, bromine Bicarbonate Sulphate
Urinary tract	Oligomineral (low mineral content) Bicarbonate
Gastrointestinal	Bicarbonate Sulphate Salt
Dermatological	Salt, bromine and iodine Radioactive Bicarbonate Sulphurous
Rheumatic diseases	Sulphurous Salt, bromine and iodine Radioactive

## THERMAL HYDROTHERAPY OR CRENOTHERAPY TECHNIQUES

### BALNEOTHERAPY

Thermal water has properties and effects that make balneotherapy one of the most common thermal treatments. With balneotherapy, thermal water has a curative effect because of its special composition and the effect of specific stimuli, such as heat, mechanical stimuli, physical and chemical action. As regards heat, it is worth noting that water, having the highest specific heat, a low conductivity coefficient and the possibility to be used in large amounts, has a great capacity to retain heat. Bodies with high heat-retention capacity are extremely useful in treating patients, because they can transfer heat in the best possible manner, that is, progressively, with no sudden changes, avoiding abrupt heat loads for the tissues in contact with the water.<sup>71</sup>

In practical terms, there are basically three types of baths:

<sup>69</sup> *Medicina Termale*, Solimene, Bruttomesso, p. 137

<sup>70</sup> *Medicine thermal*, P. Queneau, M. Boulangé, A. Françon, B. Graber-Duvernay, C. Laroche, J. Oudot, C. Roques, Masson, pp. 55-178

<sup>71</sup> *Medicine thermal*, P. Queneau, M. Boulangé, A. Françon, B. Graber-Duvernay, C. Laroche, J. Oudot, C. Roques, Masson, p. 224

- low mineral content or hypotonic baths;
- medium mineral content baths;
- high mineral content or hypertonic baths.

This classification is done based on the temperature and the salt concentration of the mineral water used. There are three specific actions related to the salt content of the water: first, boosting heat through the direct relation of the specific weight with the thermal capacity and the heat retention capacity; the second is boosting hydromechanical action; the third takes place on the hydrolipidic film, especially with hypertonic baths, with nervous stimulation, modification of osmotic flows etc. which lead to internal organ stimulation.

Sulphurous water, salt bromine and iodine water and radioactive water are best and most commonly used for rehabilitation with loco-motor diseases. The bath involves the full immersion of the body in water, with only the head out of the water. The bath technique, its duration, what is done during or after, differ according to the temperature of the water.

Cold baths are always given at a temperature between 7 and 20°C. The colder the water, the shorter the duration. At any rate, the application should never exceed 30 seconds. After the bath, the patient should be patted dry with a sponge, then rubbed vigorously with a rough, dry sheet. This immersion cold bath is used as an anti-thermal treatment for certain infectious diseases. It stimulates nerve functions as well as the excretory ones of the skin and kidneys.

Warm or temperate baths can be longer, ranging from minutes to hours.

Warm baths causes a sense of relaxation and a sweet sensation of heat, it gives back elasticity to the muscles, it dissipates tiredness and improves overall body function.

Other common balneotherapy techniques include: hydromassage (a method that exploits the pressure of water, which is maintained at a constant temperature), hydropressotherapy (jets of hot/cold thermal water manually directed to the whole body) and cardiovascular circuits (these consist of a special pool divided into two parts, the first with hot thermal water and the second with cold water).<sup>72</sup>

## **PELOID OR MUD THERAPY**

Peloid is natural or artificial mud obtained by mixing water (thermal, sea or lake/river) with inorganic, organic or mixed materials, derived from geological or biological processes. Such mud is used for packs or baths. Peloids include muds, silt, peat or moulds. In general muds are indicated for rheumatism and arthropathies and the related pain.

In thermal spas, the application of mud on the body, performed by expert hands, is done to the skin of the area(s) to be treated in a 3-10 cm thick layer, at a temperature of 45-50°C. Patients, who receive the treatment in the morning and preferably on an empty stomach, are subsequently

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<sup>72</sup>*Manuale di Medicina Termale*, Agostini, p. 49-50; *Medicina Termale*, Solimene, Bruttomesso, p. 67-69; *Trattato di idroclimatologia clinica I*, Messina, p. 590-593

covered with sheets, cellophane and blankets to reduce heat dispersion. The duration of each application is 15-20 minutes. There are various types of application, depending on the extension and the location of the mud on the body:

- Full body mud pack, which covers the whole body with the exception of the head, the front of the neck and the precordial area;
- Partial body mud pack, which can be applied to individual joints or body parts;
- Abdominal mud packs, where the mud is spread on the lumbar and abdominal regions (e.g. liver mud, mud in the abdominal-pelvic region).

At the end of the session, patients receive either a cleansing bath or a shower with normal or thermal water at a temperature between 37-40°C. Subsequently, the patient goes to a cabin (individual or with other people) where, suitably covered, he/she rests for 30-60 minutes lying down or reclined. This stage of treatment is called "reaction".

The biological and therapeutic effects are fundamental and are obtained due to:

- anti-inflammatory effect;
- analgesic effect;
- myorelaxant effect;
- trophic effects;
- increased resistance to exogenous and endogenous pathogens;
- stimulating effect on many metabolic processes;
- improvement of coenaesthesia.

Peloid treatment is especially good for primary and secondary osteoarthritis or problems related to osteoporosis, herniated discs, ankylosing spondylitis, common lumbar pain, peri-arthritis, extra-articular rheumatism, tendonitis and fibrositis. Intestinal diseases can also be treated with muds, but in such cases peloid therapy is always accompanied by drinking mineral water and other thermal techniques. Mud therapy is suitable for peripheral vessel disease, such as phlebopathy, for some skin conditions (ulcers and skin dystrophy) and other gynaecological issues.<sup>73</sup>

## **HYDROPINOTHERAPY**

This treatment involves drinking mineral water. The term comes from the Greek *idro* (water) and *pino* (drink). It consists of drinking a given

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<sup>73</sup>*Manuale di Medicina Termale*, Agostini, p. 53-54; *Medicina Termale*, Solimene, Bruttomesso, p. 44-56



amount of liquid at a pre-determined temperature at regular intervals throughout the day.<sup>74</sup>

Hydropinotherapy is recommended for treating urinary tract disorders, or intestinal diseases and in general for gastroenteric problems.

Hydropinotherapy is contraindicated in case of an obstructed urinary tract, severe kidney failure and heart failure.

The biological effect of drinking mineral water during meals can influence physiological and pathological processes. The correct use of some mineral water during normal meals can be a useful aid for certain specific health conditions, such as kidney or gallbladder stones.<sup>75</sup>

## INHALATION TREATMENT

Thermal water can also be useful to treat chronic states of inflammation and irritation of the upper and lower respiratory tracts. Thermal inhalation treatment can be administered in many different ways, depending on the intended result and can be classified according to various factors. Some of these include the chemical properties of the mineral waters used; the physical characteristics of the substances inhaled; the suitability of the devices and the delivery mechanisms. Inhalation treatment is generally classified as follows:

- ambient inhalation of gas, vapour or nebulized water (humid fog);
- direct jet inhalations, i.e. individual inhalation of gas, vapour and nebulized water (humid inhalation);
- dry inhalation (dry inhalers).<sup>76</sup>

## IRRIGATION

Irrigations consist of bringing water into contact with the mucus membranes of open cavities in the body. Water that runs and flows out at low pressure through specific cannulae comes from special containers where it is adequately mixed at the desired temperature and pressure.

There are different types: nasal, indicated for catarrhal and atrophic rhinitis and ozena; oral cavity irrigations, indicated for periodontitis, chronic dental disease and pharynx infections; vaginal irrigations are for the treatment of chronic inflammation of the vagina, cervix and Fallopian tubes as well as helping prevent tube adhesions; intestinal irrigations are used to treat some colon diseases.<sup>77</sup>

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<sup>74</sup>*Manuale di Medicina Termale*, Agostini, p. 41-44;

<sup>75</sup>*Medicina Termale*, Solimene, Bruttomesso, p. 75-77;

<sup>76</sup>*Manuale di Medicina Termale*, Agostini, p. 44-48; *Medicina Termale*, Solimene, Bruttomesso, p. 100-106; *Trattato di idroclimatologia clinica I*, Messini, p. 605-606

<sup>77</sup>*Manuale di Medicina Termale*, Agostini, p. 51-52; *Medicina Termale*, Solimene, Bruttomesso, p. 90-96; *Trattato di idroclimatologia clinica I*, Messini, p. 628-636

## **USE OF OTHER NATURAL METHODS**

In addition to the methods described thus far, there are other traditional methods that are often included under crenotherapy practices, even though there is no general consensus on this. The following can be considered as part of crenotherapy: psammotherapy (sand bathing), hydrokinesitherapy or rehab in water and speleotherapy.

### **PSAMMOTHERAPY**

Psammotherapy is an external thermal therapy that uses dry heat. It uses sand and the specific active ingredient of sea water, where the salt granules adhere to the sand grains.

Sand is the product of the fragmentation of minerals derived from the disintegration of limestone and silicate rocks due to the action of the elements and water. In this process, the heat from solar radiation plays a key role in shaping the sand grains.

Depending on its mineral composition, sand can be classified as silicate, limestone-silicate and limestone.

Sand has a specific chemical composition. It basically consists of grains and air between them (porous system), so it is a system with low thermal conductivity and limited specific surface area, which means it is able to transfer the heat it receives from solar radiation without causing burning despite the high temperature.

Sand baths are generally done outdoors, with a hole that is 20-30 cm deep, and 2 by 1 m in size. At the bottom, at least 15 layers of dry sand are prepared, while at the edges, enough sand is prepared to fully cover the patient's body.

The temperature of the sand which is applied to the body is 50-60°C and the thickness of the layer generally never exceeds 3-7 cm to allow for sun radiation to warm the sand evenly. Patients are then fully covered with a thin layer of sand so as to avoid the excessive cooling of the sand in contact with the skin.

Each session lasts from 20 to 40 minutes. It is followed by a 20 minute reaction period, which is in specific rooms (individual or collective). In specific sand bathing centres, sand baths are generally done in combination with balneotherapy using warmed sea water (37-38°C for 20 minutes) in specific tubs and pools or directly in the sea.

Psammotherapy has a biological effect due to a number of mechanisms linked to the:

- thermal effect, that is, a non-specific general or local action linked to heat (thermal therapy);

- chemical-mineral effect, that is, the biological effect due to the chemical-physical composition of the sand used;
- climatotherapy effect, that is, a biological effect produced by the seaside climate of the place where sand baths are given.

The main treatment indications for psammotherapy are similar to those for mud therapy: osteoarthritis, sequelae of traumatic injuries (fractures, distortions etc.), extra-articular rheumatisms, chronic inflammatory rheumatism etc.

## **HYDROKINESITHERAPY**

About thirty years ago, this branch of rehabilitation medicine acquired a specific identity, with the introduction of scientific studies design to define precise clinical indications and protocols for each disease.

Currently, rehabilitation in water is a fundamental way of ensuring modern and valid functional recovery for orthopaedic and neurological conditions.

Rehabilitation in water is based on Archimedes principle which indicates that the upward buoyant force exerted on a body immersed in a fluid is equal to the weight of the fluid that the body displaces, so that the more the body is immersed the lighter it is.

For example, the weight of the human body immersed vertically is apparently reduced to 95% of the real weight when it is immersed up to the calves, 80% when the water is up to the thighs, 50% up to the belly button, 20% up to the armpits, 7% at the neck and 3% when it is completely immersed.

It is clear that this makes movement in the water easier, compared to the outside environment, when the damage caused by traumas, cerebrovascular episodes or orthopaedic surgery (fractures, replacement prosthesis etc.) would make it difficult, if not impossible, to load all the body weight on the limbs.

The water in rehab pools is kept at a temperature between 34 and 36°C. There is general consensus on the fact that at this temperature the baths produce the following effects:

- myorelaxant effect, with a reduction of the muscle tone that facilitates movement, due to the direct action of heat on the muscle spindles. In this way, muscles are less sensitive to stretching with a reduction in alpha fibre activity and consequent muscular contraction. In addition, heat indirectly stimulates the skin's thermal receptors, reducing muscular contractures;

- antalgic effect, due to the increase in the pain threshold, which makes it possible to do more aggressive exercise than out of the water.<sup>78</sup>

## **SPELEOTHERAPY**

Speleotherapy is a method that exploits the microclimate of natural cavities inside a rocky layer for treatment purposes. A key advantage of such an environment is that, once one is relatively far inside the cave, there is a microclimate. Each cave is characterized by the presence of traces of gases, thermal ions and a given level of radioactivity.

### **Caves**

The distinct trait of hot-humid caves is that a thermal spa either runs through them or they are in direct contact with it. This means the relative humidity rate is very high, and the temperature can range between 20 to 70°C. One of the consequences of the high humidity level (close to saturation) is the removal of atmospheric particles by the water stem which condense around the particles and quickly deposit on the ground or walls.

In terms of HT, the effects of humidity and temperature merge with those of the thermal gas released by the water.

### **Hot Caves**

In such underground cavities the heat comes from a thermal aquifer underneath the cave system, meaning the level of humidity is lower. This is in contrast to the caves where hydrothermal action underlies the heating. Here, too, the absence of potential pathogens and the positive effects of speleotherapy are key elements.

The patient starts in the outermost zone, where the temperature is mildest and then moves inwards, through the hotter, more internal areas, staying for the prescribed amount of time at each point.

The reactions of bodily tissues through sweating and dilation/contraction of the blood vessels enable speleotherapy treatments to stimulate the neurovegetative system, metabolic exchange processes and the release of inflammatory and analgesic substances as well as activating the immune system. Moreover, the cave's micro-climate along with the high temperature and the aerosol agents can also help the upper and lower respiratory tracts.<sup>79</sup>

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<sup>78</sup>*Medicina Termale*, Solimene, Bruttomesso, p. 113-114

<sup>79</sup>*Manuale di Medicina Termale*, Agostini, p. 61-62; *Medicina Termale*, Solimene, Bruttomesso, p. 60-66

## POTENTIAL SIDE EFFECTS OF HYDROTHERAPY AND CRENOTHERAPY

All of hydrotherapy/crenotherapy practices depend very much on individual reactions. So, it is fundamental to proceed gradually with tests and if the patient has a strong reaction, a gradual tolerance should be built up. In general, the elderly, sclerotics, and patients with kidney or heart problems should not be exposed to cold hydrotherapy/crenotherapy, because it can cause dangerous hypertensive reactions. Showers are contraindicated in states of excitement. During pregnancy, abdominal showers should be avoided and the use of hot water is generally not advisable. Baths are contraindicated in cases of weakness, breakdown or if there is a risk of bleeding. Equally cold baths are not recommended for patients with a fever. Very hot baths should be avoided in all cases, but especially for the elderly or those who might have latent cardiovascular lesions.<sup>80</sup>

However, although the side effects of hydrotherapy/crenotherapy treatments are generally mild, in some cases they can be unexpected. Such effects might be the result of improperly administered treatments, however, in most cases, they are the result of individual reactions to treatment.

Some of the most common side effects of treatments are:

- headache (from an intense or excessively long treatment);
- dizziness;
- irritability;
- localized or generalized pain;
- insomnia;
- nausea;
- heart palpitations;
- weakness;
- cold.

## CONTRAINDICATIONS TO HYDROTHERAPY AND CRENOTHERAPY

A few words should be said about contraindications to hydrotherapy/crenotherapy. These can be divided into relative and absolute. Relative contraindications refer to a specific method or form of delivery for a given disease; while absolute contraindications mean it is not advisable to expose patients suffering from certain diseases to the treatment. Actually, many studies and authors do not agree with this distinction and state that any contraindications are always relative. Out of

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<sup>80</sup> *Medicine thermal*, P. Queneau, M. Boulangé, A. Françon, B. Graber-Duvernay, C. Laroche, J. Oudot, C. Roques, Masson, p. 47

caution, though, the absolute contraindications are included below. First, there are patients with cancer or those who have had recent cancer resection surgery. Hydrotherapy/crenotherapy is contraindicated in cases of kidney failure, heart failure, severe hypertension, and severe organ diseases such as cirrhosis and immunodeficiency.<sup>81</sup>

Hydrotherapy/crenotherapy should not be used in case of fever and, to protect the health of other users of thermal centres, in case of infectious disease.<sup>82 83</sup>

## CONCLUSIONS

HT is a very ancient therapeutic method, consisting of many techniques that, over the centuries, have seen numerous developments. Today, this practice is not only used to treat many disorders and diseases, but also in rehabilitation and to improve the quality of life in general.

There are many scientific articles that describe the techniques, especially balneotherapy, for different conditions of orthopaedic, cardiological or angiological nature. Physiotherapy and gastroenterology have also shown interest in these practices. This shows the extent of the indications that traditionally have been considered for this method. The methods used, in addition, are simple and inexpensive, however they require adequate training and supervision by qualified staff to ensure safety and efficacy.

More recently, alongside the considerations from the traditional use of these methods, a sizable body of scientific study is being developed and is producing evidence which is needed for the safe, effective and adequate administration of these treatments. This element certainly poses a challenge which requires a special effort from the professionals working in this sector, with a view to moving from the century-old HT practices to a modern and scientific HT.

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<sup>81</sup> *Medicine thermal*, P. Queneau, M. Boulangé, A. Françon, B. Graber-Duvernay, C. Laroche, J. Oudot, C. Roques, Masson, p. 233

<sup>82</sup> *Medicina Termale*, Solimene, Bruttomesso, p. 119-120

<sup>83</sup> *Vademecum of spanish mineral-medicinal waters*, Instituto de Salud Carlos III, p. 33

## **STATUS OF HYDROTHERAPY EVIDENCE**

### **NEED FOR A DATA ASSESSMENT**

HT started in the Mediterranean area many centuries ago and soon developed in all the areas that were under the rule of the Roman Empire. However, some forms of HT can be traced, since ancient times, to just about all parts of the world, from Japan to Iceland, and from North Africa to North America.

HT is not only very much appreciated by the peoples in the countries where it developed, but it is also officially recognized by the governments of many countries and is part of the national healthcare services.

Despite a long and well documented history, there is still a good deal of scepticism about its efficacy, especially among the scientific communities and physicians that base their practices only on western biological medical sciences.

Indeed, there is a hot debate on whether HT actually works as a treatment or if its effects are mainly a placebo or are caused by uncritical patient expectations.

This work intends to carry out a preliminary exploration to find out whether there are good quality scientific studies published in English in international literature that can be found using standard search engines. The objective is precisely to verify if such studies are able to document beyond any doubt through a base of solid evidence, the superior efficacy of HT versus a placebo or the equivalence with the standard of care for a given disease.

### **METHODOLOGICAL CONSIDERATIONS**

Unlike what happens with the assessment of a new drug, with HT, organizing controlled clinical trials is rather difficult, especially if we want to have a placebo control in a double blind study design. The smell of the water, the perception of mud, and the experience of immersion are but a few factors that make it very hard to have a real placebo and a truly blind study. Furthermore, the use of a placebo for diseases in which HT has proven effective could be judged very critically from an ethical standpoint.

A simpler way for comparing the efficacy of HT to standard treatments could be to create perfectly equivalent, randomized groups where one would be exposed to HT and the other conventional medicine.

It would be very useful also to involve groups that receive no treatment. However, it should be taken into account that some diseases, for which

HT is very commonly used, such as arthrosis, tend to develop positively even without treatment.

Retrospective analyses, observational studies, non-randomized and non-controlled studies can have some value in defining experimental hypotheses that then need to be further assessed. However, they certainly are not sufficiently reliable to provide general treatment indications. They should be taken into consideration only for diseases where no other type of treatment is available.

Assessing HT practices to reach shared, clear and universally accepted conclusions is far from an easy task.

In addition, although the efficacy of HT is still being questioned, other aspects, such as safety and cost-benefits, should be taken into account.

Indeed, given equal efficacy, these elements could play a role in choosing HT for treating certain conditions.<sup>84</sup>

## **SAFETY**

Generally speaking, HT can be considered as a safe treatment, provided it is administered by adequately trained professionals. In addition, unlike drugs, it is not toxic and adverse events are minimal. This is probably the reason why using HT in treating chronic pain is so popular in many countries.

Although HT is sometimes less effective than standard drugs, its use should really be taken into consideration given its safety. For this reason, despite the difference in efficacy, HT should be taken into due account in the treatment strategies for diseases that require strong and toxic drugs, so that doses and frequency of administration can be reduced.

## **STUDIES ON THE ACTION MECHANISM**

Obviously, it is important to assess whether a treatment works, but it is equally important to understand the underlying mechanism which accounts for the effects of a treatment. Apart from the scientific interest, this can provide useful information on the efficacy and on the potential extension of the application to other fields, and also on the adequacy of use.

Clinical trials can precede the studies on the action mechanism, but sometimes the opposite is true. For instance, some studies on the effects

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<sup>84</sup> WHO, *General Guidelines for Methodologies on Research and Evaluation of Traditional Medicine*, available online at: [http://whqlibdoc.who.int/hq/2000/WHO\\_EDM\\_TRM\\_2000.1.pdf](http://whqlibdoc.who.int/hq/2000/WHO_EDM_TRM_2000.1.pdf), visited on 14 may 2013



of heat sometimes came before the application of HT to the treatment of musculoskeletal diseases.

Modern scientific research has documented the following effects of HT:

- antalgic;
- myorelaxant;
- activation of microcirculation;
- immunomodulation;
- neuro-hormonal stimulation;
- modulation of fat and carbohydrate metabolism.

However, although mechanistic trials have developed considerably, further research confirmed by independent groups would still be very important in this field.

## **SELECTION OF CLINICAL TRIALS**

Over the past few years, many clinical trials have been produced. However, this work only took into consideration the publications that meet one of the following requirements:

- Meta analyses and systematic reviews, considered as the highest possible level of evidence, provide on the one hand a solid evidence base for clinical practice, and on the other show the richness of base research. Without randomized, controlled clinical trials, indeed, it would be impossible to carry out meta analyses and systematic reviews.
- Randomized and controlled clinical trials provide the basic evidence for using this treatment for individual diseases or disorders. The quality of trials varies a lot, partly depending on the design of the study. As already mentioned, in HT there is an objective difficulty in defining the placebo.
- Observational studies can either be perspective or retrospective. In general, they are not randomized but there is some form of control. They are useful in assessing the safety of a procedure and offer a preliminary assessment for the definition of hypotheses that subsequently will need to be validated through randomized, controlled clinical trials.
- Basic studies consist of studies on the basic action mechanisms of a certain treatment. They can be useful to explain the efficacy of a given treatment both to extend the scope of application or to identify more appropriate applications of that treatment.

This research has been done on the following search engines: Pubmed, WEB of Science, Cochrane Library. However, PubMed contained most of the papers we identified, so it has been used as the main source.

### CARDIOVASCULAR SYSTEM

Type of studies	N° lxt	Title	Authors
Meta-analyses and systematic reviews			
Randomized studies	<u>2</u>	Beneficial effects of Waon therapy on patients with chronic heart failure: results of a prospective multicenter study	Miyata M et al
Observational studies	<u>3</u>	Improvement of autonomic nervous activity by Waon therapy in patients with chronic heart failure	Kuwahata S et al.
	<u>4</u>	Waon therapy improves the prognosis of patients with chronic heart failure	Kihara T et al.
	<u>5</u>	Effect of Waon therapy on oxidative stress in chronic heart failure	Fujita S et al.
	<u>7</u>	Effect of repeated sauna treatment on exercise tolerance and endothelial function in patients with chronic heart failure	Ohori T et al.
Basic studies	<u>1</u>	Waon therapy for cardiovascular disease: innovative therapy for the 21st century	Miyata M et al.
	<u>6</u>	Waon therapy mobilizes CD34+ cells and improves peripheral arterial disease	Shinsato T et al.

## SKIN AND ANNEXES

Type of studies	N° lxt	Title	Authors
Meta-analyses and systematic reviews	<a href="#">8</a>	[Psoriasis. Natural versus artificial balneophototherapy]	Roos S et al.
Randomized studies	<a href="#">1</a>	Balneotherapy for atopic dermatitis in children at Comano spa in Trentino, Italy	Farina S et al.
	<a href="#">5</a>	A first prospective randomized controlled trial on the efficacy and safety of synchronous balneophototherapy vs. narrow-band UVB monotherapy for atopic dermatitis	Heinlin J et al.
	<a href="#">9</a>	Balneophototherapy of psoriasis: highly concentrated salt water versus tap water--a randomized, one-blind, right/left comparative study	Gambichler T et al.
	<a href="#">10</a>	A pragmatic randomized controlled trial on the effectiveness of highly concentrated saline spa water baths followed by UVB compared to UVB only in moderate to severe psoriasis	Brockow T et al.
	<a href="#">13</a>	A randomized clinical trial in psoriasis: synchronous balneophototherapy with bathing in Dead Sea salt solution plus narrowband UVB vs. narrowband UVB alone (TOMESA-study group)	Klein A et al.
	<a href="#">15</a>	A randomized controlled comparison of the efficacy of Dead Sea salt balneophototherapy vs. narrowband ultraviolet B monotherapy for chronic plaque psoriasis	Dawe RS et al.
	<a href="#">16</a>	A pragmatic randomized controlled trial on the effectiveness of low concentrated saline spa water baths followed by ultraviolet B (UVB) compared to UVB only in moderate to severe psoriasis	Brockow T et al.
	<a href="#">18</a>	Saline spa water or combined water and UV-B for psoriasis vs conventional UV-B: lessons from the Salies de Béarn randomized study	Léauté-Labrèze C et al.
	<a href="#">19</a>	Bath PUVA and saltwater baths followed by UV-B phototherapy as treatments for psoriasis: a randomized controlled trial	Schiener R et al.
	<a href="#">20</a>	Immediate and delayed effects of treatment at the Dead Sea in patients with psoriatic arthritis	Elkayam O et al.
Observational studies	<a href="#">2</a>	Climatotherapy of atopic dermatitis at the Dead Sea: demographic evaluation and cost-effectiveness	Harari M et al.
	<a href="#">3</a>	Climatotherapy at the dead sea: an effective treatment modality for atopic dermatitis with significant positive impact on quality of life	Adler-Cohen C et al.

Type of studies	N° lxt	Title	Authors
	<a href="#">4</a>	Dead Sea treatment - principle for outpatient use in atopic dermatitis: safety and efficacy of synchronous balneophototherapy using narrowband UVB and bathing in Dead Sea salt solution	Schiffner R et al.
	<a href="#">6</a>	[Comparison of balneophototherapy and UVA/B mono-phototherapy in patients with subacute atopic dermatitis]	Dittmar HC et al.
	<a href="#">7</a>	Bathing in a magnesium rich Dead Sea salt solution improves skin barrier function, enhances skin hydration and reduces inflammation in atopic dry skin	Proksch E et al.
	<a href="#">11</a>	Synchronous balneophototherapy is effective for the different clinical types of psoriasis	Holló P et al.
	<a href="#">12</a>	Quality of life of psoriasis patients before and after balneo -- or balneophototherapy	Tabolli S et al.
	<a href="#">14</a>	Evaluation of a multicentre study of synchronous application of narrowband ultraviolet B phototherapy (TL-01) and bathing in Dead Sea salt solution for psoriasis vulgaris	Schiffner R et al.
	<a href="#">26</a>	[Effect of treatment with salt from the Dead Sea (Tomesa therapy) on epidermal Langerhans cells--a clinical study]	Gruner S et al.
Basic studies	<a href="#">21</a>	Skin penetration of minerals in psoriatics and guinea-pigs bathing in hypertonic salt solutions	Shani J et al.
	<a href="#">22</a>	Inhibition of proliferation of psoriatic and healthy fibroblasts in cell culture by selected Dead-sea salts	Levi-Schaffer F et al.
	<a href="#">23</a>	Penetration of selected Dead Sea minerals through a healthy rabbit skin, from a sustained-release transparent varnish, as a prospective treatment for psoriasis	Jashovam Shani et al.
	<a href="#">24</a>	Effect of Dead-Sea brine and its main salts on cell growth in culture	Shani J et al.
	<a href="#">25</a>	Magnesium ions inhibit the antigen-presenting function of human epidermal Langerhans cells in vivo and in vitro. Involvement of ATPase, HLA-DR, B7 molecules, and cytokines	Schempp CM et al.
	<a href="#">27</a>	[Inflammation-inhibiting effect of magnesium ions in contact eczema reactions]	Greiner J et al.
	<a href="#">28</a>	Sulphurous medicinal waters increase somatostatin release: It is a possible mechanism of anti-inflammatory effect of balneotherapy in psoriasis	Boros M. et al.
	<a href="#">29</a>	Hydrogen sulfide impairs keratinocyte cell growth and adhesion inhibiting	Giuliana G et al.

Type of studies	N° lxt	Title	Authors
		mitogen-activated protein kinase signaling	

### MUSCULOSKELETAL SYSTEM

Type of studies	N° lxt	Title	Authors
Meta-analyses and systematic reviews	<u>1</u>	Balneotherapy for osteoarthritis	Verhagen AP et al.
	<u>2</u>	Balneotherapy for osteoarthritis. A cochrane review	Verhagen A et al.
	<u>3</u>	Short- and long-term therapeutic effects of thermal mineral waters in knee osteoarthritis: a systematic review of randomized controlled trials	Harzy T et al.
	<u>4</u>	Balneotherapy for rheumatoid arthritis	Verhagen AP et al.
	<u>5</u>	The Effectiveness of Hydrotherapy in the Management of Rheumatoid Arthritis: A Systematic Review	Al-Qubaeissy KY et al.
	<u>6</u>	The effectiveness of hydrotherapy in the management of fibromyalgia syndrome: a systematic review	McVeigh JG et al.
	<u>7</u>	Effectiveness of aquatic exercise and balneotherapy: a summary of systematic reviews based on randomized controlled trials of water immersion therapies	Kamioka H et al.
	<u>8</u>	Efficacy of hydrotherapy in fibromyalgia syndrome--a meta-analysis of randomized controlled clinical trials	Langhorst J et al.
	<u>9</u>	Spa therapy and balneotherapy for treating low back pain: meta-analysis of randomized trials	Pittler MH et al.
	<u>10</u>	Short- and long-term therapeutic effects of thermal mineral waters in knee osteoarthritis: a systematic review of randomized controlled trials	Harzy T et al.
	<u>11</u>	The therapeutic effect of balneotherapy: evaluation of the evidence from randomised controlled trials	Falagas ME et al.
	<u>12</u>	[Methodological reflections on 20 randomized clinical hydrotherapy trials in rheumatology]	Queneau P et al.
	<u>13</u>	[Balneotherapy and spa therapy of rheumatic diseases in Turkey: a systematic review]	Karagülle MZ et al.
	<u>14</u>	[New evidences on spa therapy in fibromyalgia]	Giannitti C et al.
	<u>15</u>	Efficacy of hydrotherapy in fibromyalgia syndrome--a meta-	Langhorst J et al.

Type of studies	N° lxt	Title	Authors
		analysis of randomized controlled clinical trials	
	<a href="#">16</a>	[Spa therapy in rheumatology. Indications based on the clinical guidelines of the French National Authority for health and the European League Against Rheumatism, and the results of 19 randomized clinical trials]	Françon A et al.
	<a href="#">17</a>	Taking baths: the efficacy of balneotherapy in patients with arthritis. A systematic review	Verhagen AP et al.
	<a href="#">18</a>	Crenobalneotherapy for limb osteoarthritis: systematic literature review and methodological analysis	Forestier R et al.
	<a href="#">19</a>	The Effectiveness of Hydrotherapy in the Management of Rheumatoid Arthritis: A Systematic Review	Al-Qubaeissy KY et al.
	<a href="#">20</a>	Balneotherapy for rheumatoid arthritis	Verhagen AP et al.
	<a href="#">21</a>	Balneotherapy for rheumatoid arthritis and osteoarthritis	Verhagen AP et al.
	<a href="#">26</a>	The Effectiveness of Hydrotherapy in the Management of Rheumatoid Arthritis: A Systematic Review	Al-Qubaeissy KY et al.
	<a href="#">35</a>	The effectiveness of hydrotherapy in the management of fibromyalgia syndrome: a systematic review	McVeigh JG et al.
	<a href="#">43</a>	[Spa therapy in rheumatology. Indications based on the clinical guidelines of the French National Authority for health and the European League Against Rheumatism, and the results of 19 randomized clinical trials]	Françon A et al.
	<a href="#">68</a>	Evidence-based hydro- and balneotherapy in Hungary—a systematic review and meta-analysis	Bender T et al.
Randomized studies	<a href="#">22</a>	Beneficial effects of spa treatment on functional status and quality of life of patients with rheumatoid arthritis]	Mustur D et al.
	<a href="#">23</a>	[Influence of balneophysical therapy on activity, functional capacity, and quality of life in patients with rheumatoid arthritis]	Stojanović S et al.
	<a href="#">25</a>	Mud compress therapy for the hands of patients with rheumatoid arthritis	Codish S et al.
	<a href="#">27</a>	Mud pack therapy in rheumatoid arthritis.	Sukenik S et al.
	<a href="#">29</a>	Dead Sea bath salts for the treatment of rheumatoid arthritis	Sukenik S et al.
	<a href="#">30</a>	Effects of mud-bath treatment on fibromyalgia patients: a randomized clinical trial	Fioravanti A et al.
	<a href="#">32</a>	Effects of balneotherapy on serum	Ardıç F et al.

Type of studies	N° lxt	Title	Authors
		IL-1, PGE2 and LTB4 levels in fibromyalgia patients	
	<a href="#">33</a>	Thalassotherapy for fibromyalgia: a randomized controlled trial comparing aquatic exercises in sea water and water pool	de Andrade SC et al.
	<a href="#">34</a>	SPA therapy in fibromyalgia: a randomised controlled clinic study	Dönmez A et al.
	<a href="#">36</a>	Spa therapy for ankylosing spondylitis at the Dead Sea	Codish S et al.
	<a href="#">37</a>	Balneotherapy at the Dead Sea area for knee osteoarthritis	Sukenik S et al.
	<a href="#">40</a>	The effect of spa therapy in chronic low back pain: a randomized controlled, single-blind, follow-up study	Tefner IK et al.
	<a href="#">41</a>	Effectiveness of balneotherapy in chronic low back pain -- a randomized single-blind controlled follow-up study	Balogh Z et al.
	<a href="#">47</a>	Spa therapy in the treatment of knee osteoarthritis: a large randomised multicentre trial	Forestier R et al.
	<a href="#">56</a>	Therapy with mud compresses for knee osteoarthritis: comparison of natural mud preparations with mineral-depleted mud	Flusser D et al.
	<a href="#">57</a>	Does mud pack treatment have any chemical effect? A randomized controlled clinical study	Odabasi E et al.
	<a href="#">59</a>	Mud bath therapy influences nitric oxide, myeloperoxidase and glutathione peroxidase serum levels in arthritic patients	Bellometti S et al.
	<a href="#">61</a>	Both serum receptors of tumor necrosis factor are influenced by mud pack treatment in osteoarthrotic patients	Bellometti S et al.
	<a href="#">62</a>	Mud-bath treatment in spondylitis associated with inflammatory bowel disease--a pilot randomised clinical trial	Cozzi F et al.
	<a href="#">65</a>	Use of spa therapy to improve the quality of life of chronic low back pain patients	Constant F et al.
	<a href="#">66</a>	Prolonged effects of 3 week therapy in a spa resort on lumbar spine, knee and hip osteoarthritis: follow-up after 6 months. A randomized controlled trial	Nguyen M et al.
	<a href="#">69</a>	The effect of Neydharting mud-pack therapy on knee osteoarthritis: a randomized, controlled, double-blind follow-up pilot study.	Tefner IK et al.
Observational studies	<a href="#">28</a>	Sulphur bath and mud pack treatment for rheumatoid arthritis at	Sukenik S et al.

Type of studies	N° lxt	Title	Authors
		the Dead Sea area	
	<a href="#">31</a>	The efficacy of balneotherapy and physical modalities on the pulmonary system of patients with fibromyalgia	Kesiktas N et al.
	<a href="#">42</a>	Additional therapeutic effect of balneotherapy in low back pain	Dogan M et al.
	<a href="#">45</a>	Effect of balneotherapy on temporospatial gait characteristics of patients with osteoarthritis of the knee	Kiliçoğlu O et al.
	<a href="#">46</a>	A 10-day course of SPA therapy is beneficial for people with severe knee osteoarthritis. A 24-week randomised, controlled pilot study	Karagülle M et al.
	<a href="#">48</a>	[Sulphur Mineral Water and SPA Therapy in Osteoarthritis]	Costantino M et al.
	<a href="#">49</a>	[Knee osteoarthritis and SPA therapy: assessment of joint function and quality of life]	Costantino M et al.
	<a href="#">50</a>	[Sulphur mud-bath treatment in osteoarthrosis: therapeutic activity and efficiency on the quality of life]	Costantino M et al.
	<a href="#">51</a>	Short- and long-term effects of spa therapy in knee osteoarthritis	Fioravanti A et al.
	<a href="#">52</a>	Contribution of individual spa therapies in the treatment of chronic pain	Strauss-Blasche G et al.
	<a href="#">53</a>	Magnitude and duration of the effects of two spa therapy courses on knee and hip osteoarthritis: an open prospective study in 51 consecutive patients	Forestier R.
	<a href="#">54</a>	Balneotherapy in elderly patients: effect on pain from degenerative knee and spine conditions and on quality of life	Gaál J et al.
	<a href="#">60</a>	Production of matrix metalloproteinases and their inhibitors in osteoarthritic patients undergoing mud bath therapy	Bellometti S et al.
	<a href="#">63</a>	Effect on osteoarthritis of spa therapy at Bourbonne-les-Bains	Guillemin F et al.
	<a href="#">64</a>	Comparison of intra-articular hyaluronic acid injections and mud-pack therapy in the treatment of knee osteoarthritis	Bostan B et al.
Basic studies	<a href="#">24</a>	[Hydrogen sulphide water balneum effect on erythrocyte catalase activity in patients with rheumatoid arthritis--in vitro study]	Wozakowska-Kapłon B et al.
	<a href="#">38</a>	Hydrotherapy, balneotherapy, and spa treatment in pain management	Bender T et al.
	<a href="#">39</a>	Mechanisms of action of spa therapies in rheumatic diseases: what scientific evidence is there?	Fioravanti A et al.



Type of studies	N° lxt	Title	Authors
	<a href="#">44</a>	Oxidative stress, hemoglobin content, superoxide dismutase and catalase activity influenced by sulphur baths and mud packs in patients with osteoarthritis	Jokić A et al.
	<a href="#">55</a>	[Fangotherapy in chronic degenerative rheumatic diseases]	Grassi M et al.
	<a href="#">58</a>	[Beta-endorphin and stress hormones in patients affected by osteoarthritis undergoing thermal mud therapy].	Pizzoferrato A et al.
	<a href="#">67</a>	Cytokine levels in osteoarthritis patients undergoing mud bath therapy	Bellometti S et al.
	<a href="#">70</a>	Exogenous hydrogen sulfide induces functional inhibition and cell death of cytotoxic lymphocytes subsets	Prisco M et al.
	<a href="#">71</a>	Hydrogen sulfide prevents apoptosis of human PMN via inhibition of p38 and caspase 3	Rinaldi L et al.

#### RESPIRATORY SYSTEM

Type of studies	N° lxt	Title	Authors
Meta-analyses and systematic reviews			
Randomized studies	<a href="#">1</a>	Sulphurous-arsenical-ferruginous (thermal) water inhalations reduce nasal respiratory resistance and improve mucociliary clearance in patients with chronic sinonasal disease: preliminary outcomes.	Staffieri A et al.
	<a href="#">5</a>	[Clinical evaluation of the efficacy of Salsomaggiore (Italy) thermal water in the treatment of rhinosinusal pathologies].	Passali D et al.
	<a href="#">16</a>	Effect of inhalation of thermal water on airway inflammation in chronic obstructive pulmonary disease.	Pellegrini M et al
	<a href="#">21</a>	Effectiveness of Ischia thermal water nasal aerosol in children with seasonal allergic rhinitis: a randomized and controlled study.	Miraglia Del Giudice M et al.
	<a href="#">22</a>	Crenotherapy: a neglected resource for human health now re-emerging on sound scientific concepts.	Vaccarezza M et al.
	<a href="#">24</a>	[Efficacy of inhalation therapy with water of Salsomaggiore (Italy) in chronic and recurrent nasosinusal inflammation treatment].	Passali D et al.
Observational studies	<a href="#">6</a>	[Inhalation therapy with sulphur water in ORL: clinical-experimental study].	Costantino M et al.
	<a href="#">9</a>	Acute exacerbation of bronchial	Beer SI et al

Type studies	of	N° lxt	Title	Authors
			asthma in children associated with afternoon weather changes.	
		<a href="#">12</a>	SPA therapy of upper respiratory tract inflammations.	Passali D et al.
		<a href="#">23</a>	[Clinical study on 40 cases of inflammatory pathologies of upper respiratory and digestive tract treated by inhalatory crenotherapy].	Vassallo A et al.
Basic studies		<a href="#">2</a>	[Spa treatment in pediatric pneumo-allergology and ENT].	Jean R et al.
		<a href="#">3</a>	[The curative action of Monticelli Term's water in upper respiratory tract diseases (author's transl)]	Turchi R et al.
		<a href="#">4</a>	[Hydrological indications in the therapy of pharyngitis].	Olina M et al.
		<a href="#">7</a>	[Crenotherapy in sports medicine: the state of the art].	Grassi M et al.
		<a href="#">8</a>	[Anti-inflammatory drugs in ORL].	Felisati D et al.
		<a href="#">10</a>	Effect of sulfurous (thermal) water on T lymphocyte proliferative response.	Valitutti S et al.
		<a href="#">11</a>	[Good tolerance and absence of immunologic effects in mice treated with arsenic-rich thermal water].	Mercier P et al.
		<a href="#">13</a>	Free radical-scavenging activity of sulfurous water investigated by electron paramagnetic resonance (EPR) spectroscopy.	Braga PC et al.
		<a href="#">14</a>	Effects of sulphurous water on human neutrophil elastase release.	Braga PC et al.
		<a href="#">15</a>	Antioxidant effect of sulphurous thermal water on human neutrophil bursts: chemiluminescence evaluation.	Braga PC et al.
		<a href="#">17</a>	Clinical implications of thermal therapy in lifestyle-related diseases.	Biro S et al.
		<a href="#">18</a>	[Treatment of respiratory and ORL diseases with mineral waters in children].	Fauquert JL et al.
		<a href="#">19</a>	[Good tolerance and absence of immunologic effects in mice treated with arsenic-rich thermal water].	Mercier P et al.
		<a href="#">20</a>	Crenotherapy modulates the expression of proinflammatory cytokines and immunoregulatory peptides in nasal secretions of children with chronic rhinosinusitis.	Passariello A et al.
	<a href="#">25</a>	Impact of sulphurous water Politzer inhalation on audiometric parameters in children with otitis media with effusion	Mirandola P et al.	

## **CONCLUSIONS**

The studies that were used for this work are very diverse. They include meta-analyses, systematic reviews, controlled randomized trials, observational studies and research into action mechanisms.

The fields where most information was retrieved are also quite different: orthopaedics, cardiovascular and respiratory systems, dermatology.

Evidence in musculoskeletal disease treatment seems more solid, whereas for other areas the research methodology is often poor, recruitment unsatisfactory and study design is faulty.

The cause for such poor evidence to support HT is probably ascribable to its ancient origins. It started and developed during historical times when scientific methods were unknown. Only recently has it been assessed scientifically.

So, tradition would suggest popular uses and applications are maintained. Nonetheless, it is fundamental to develop more in-depth systematic methods of research to ensure safety and more suitable use to protect consumers.

## MONITORING SURVEY ON HYDROTHERAPY

One of the key elements of this study is the Monitoring Survey. Its purpose is to assess to what extent HT is used and how, both in countries with a long-standing thermal tradition and new comers. Below is a list of the questions and the related charts of some of the answers that were the basis for this Monitoring Survey. All in all, they provide a basic assessment of many aspects of how HT is used and whether it is part of the national healthcare service of the different countries.

### PARTICIPANTS

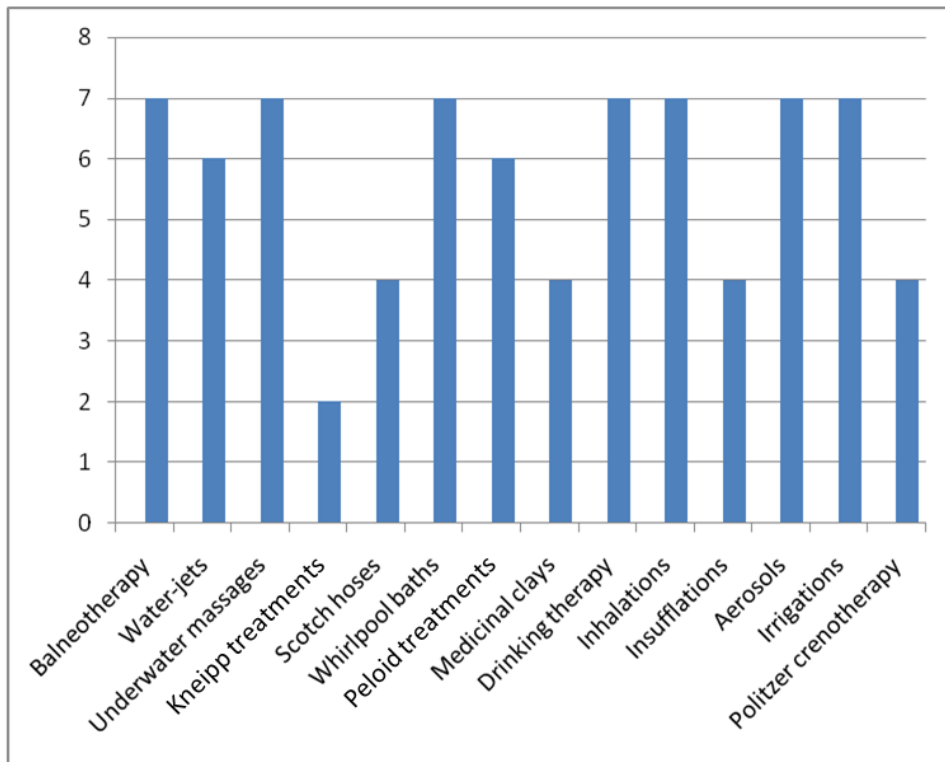
- **China:** Cao Wen Fu
- **Cuba:** Florana Menéndez Camporredondo
- **France:** Christian-François Roques Latrille
- **Hungary:** Thamas Bender
- **Italy:** Antonella Fioravanti
- **Poland:** Irena Ponikowska
- **Portugal:** Pedro Cantista
- **Romania:** Olga Surdu, MD, PhD
- **Russian Federation:** Nikolay Storozhenko; Igor Bobrovinski
- **Tunisia:** Taoufik Khalfallah

### QUESTIONS

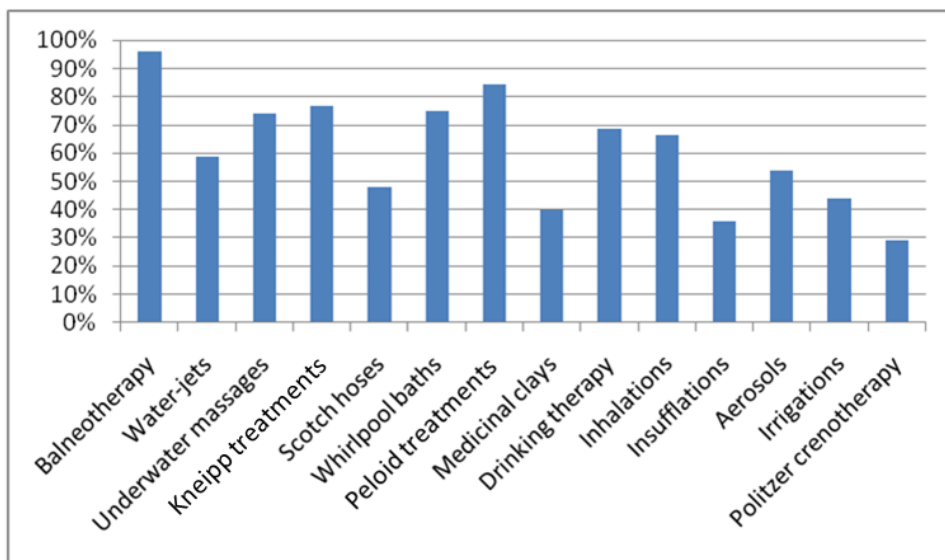
#### 1) Are there HT practices in your country?

HT is practiced in all countries. The results of this first question basically led to the conclusion that, in essence, all the countries involved practice HT in some form.

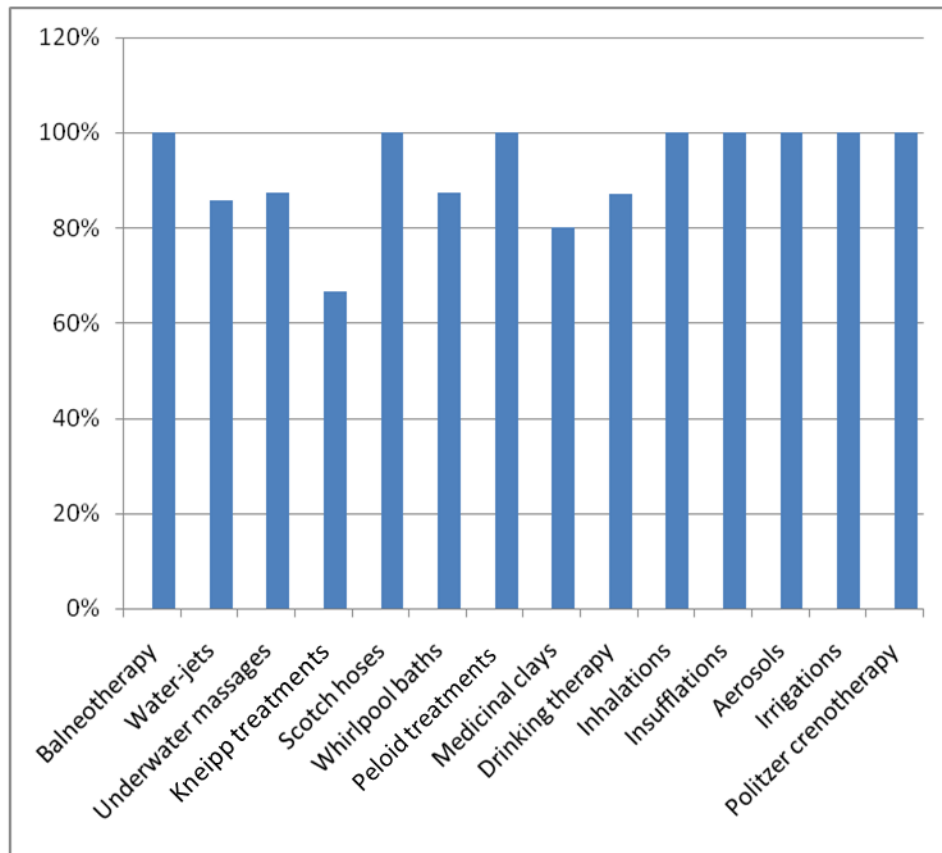
1a) What types of HT practices are there?



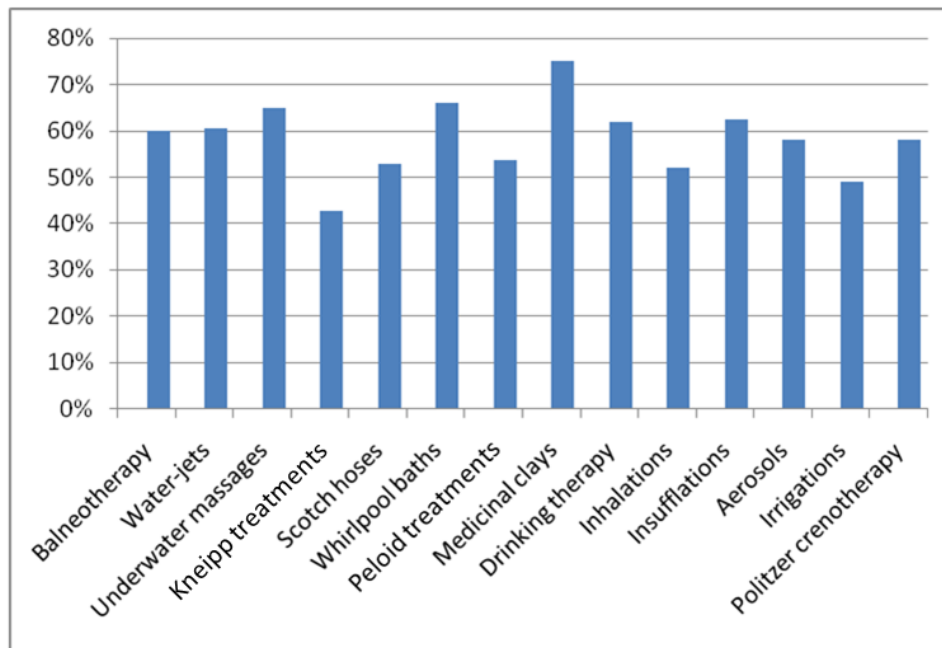
1b) Which ones are most frequently used? Indicate the percentage of use of each in the last year in your country.



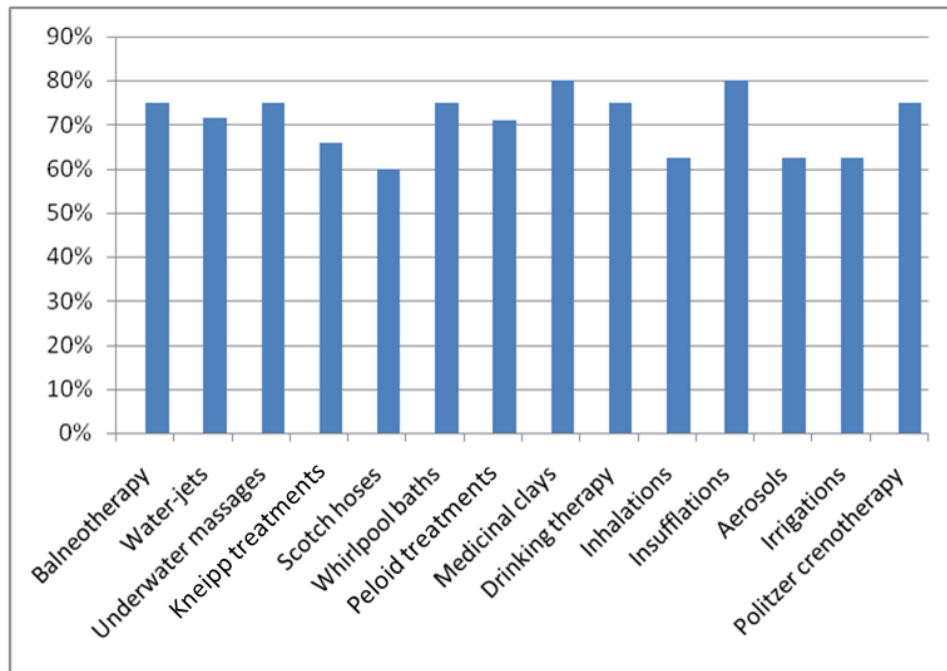
**1c) Which of these are subject to medical prescriptions?**



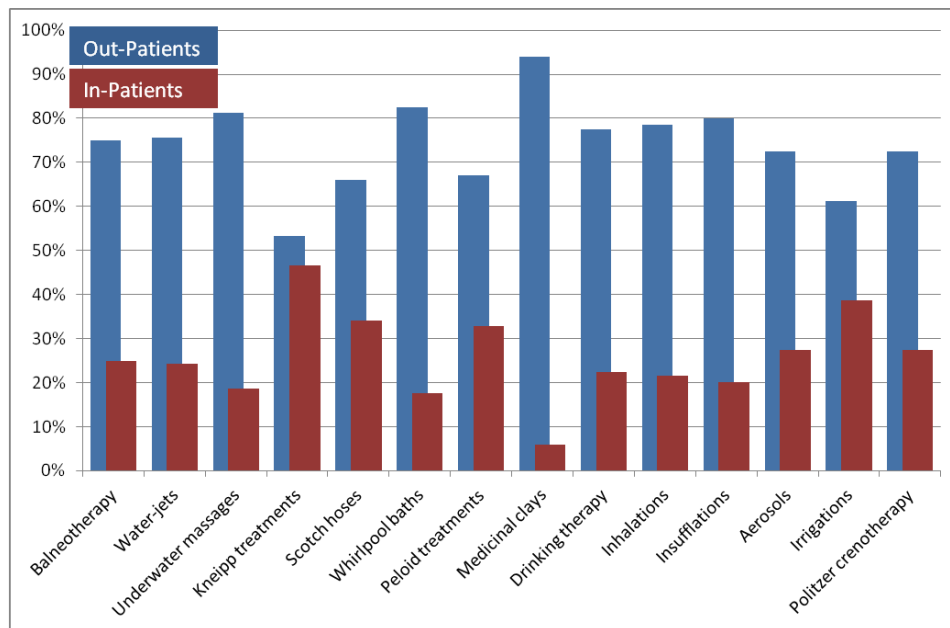
**1d) Which of these are provided under the supervision of a doctor?**



**1e) Which of these are used along with other operating models? In conjunction with other operating models?**



**1f) Which of these are used on out-patients/ in-patients?**



**2) Do the public authorities officially regulate or recognize either all of part of such therapies?**

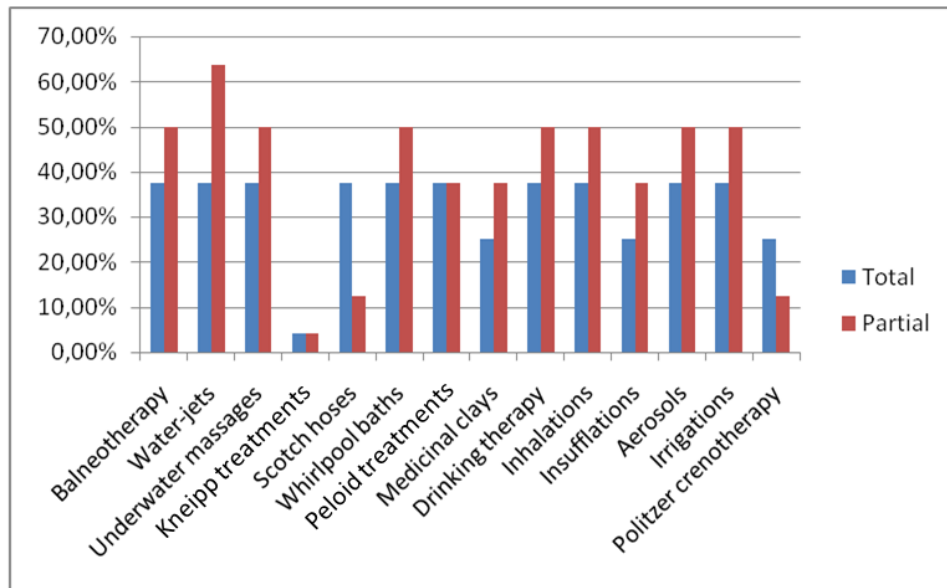
All the countries indicated official recognition for HT.

**2a) Do specific local laws regulate HT practices?**

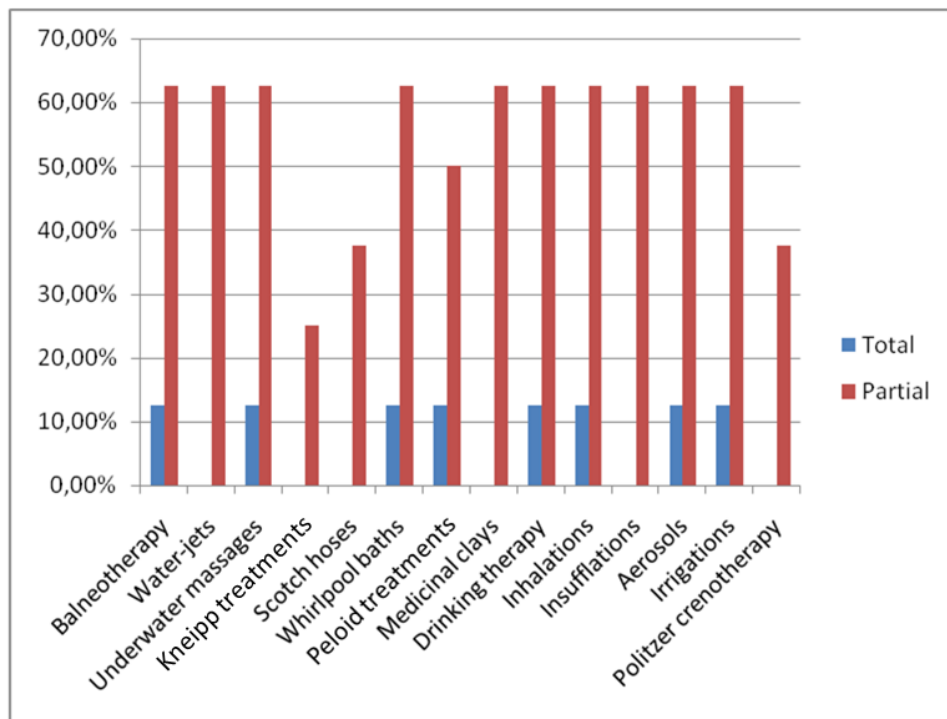
No= 12.5% of the answers

Yes = 87.5% of the answers

**2b) Does the national health service officially refund such therapies or parts of such therapies? (Total/ Partial)**

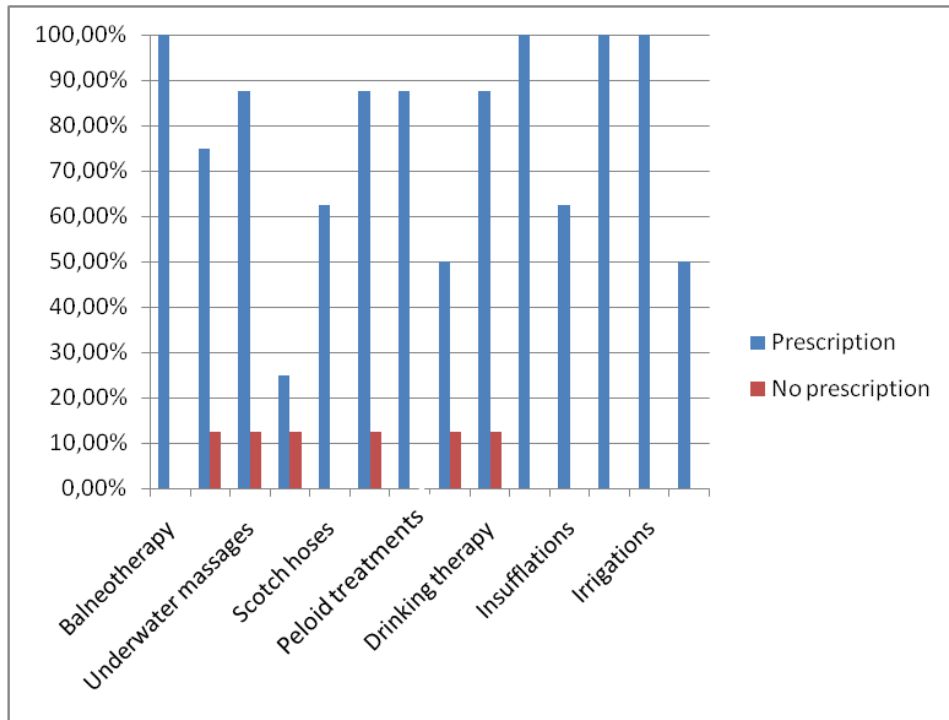


**2c) Do private insurance firms officially refund such therapies or parts of such therapies? (Total/ Partial)**

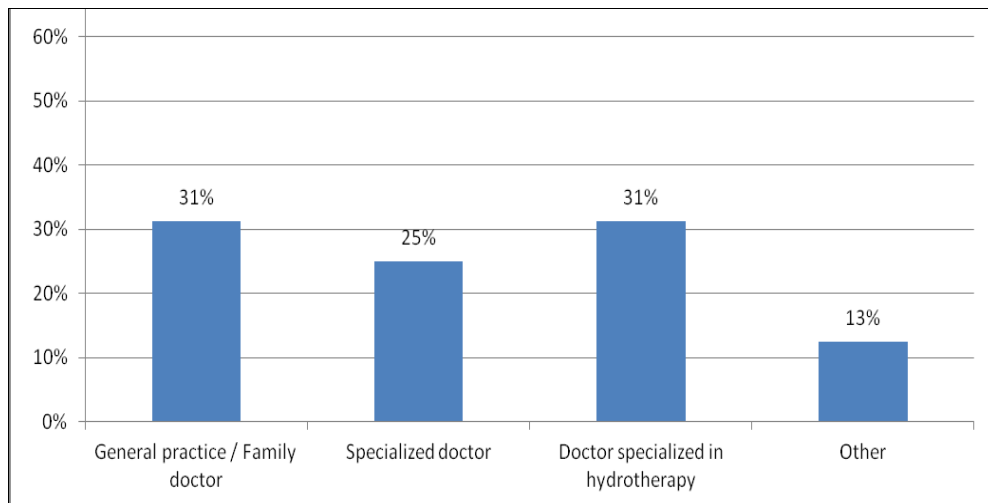




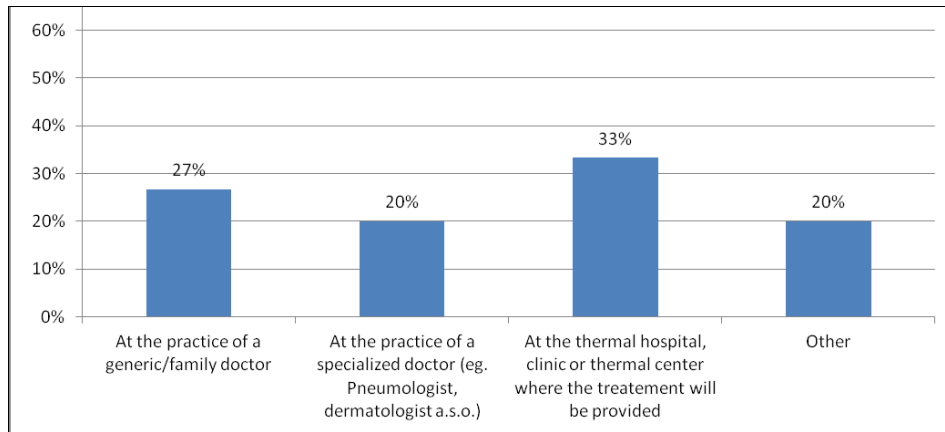
**2d) Which of these recognized practices are provided subject to a medical prescription?**



**2e) Who should prescribe HT treatment to patients?**



**2f) When are hydrological therapies prescribed?**



**3) Is HT officially accepted in your country by the scientific medical community? (Scientific medical associations)**

Yes = 100% of the answers.

**3a) Is HT officially accepted in your country by the scientific academic community? (Universities)**

Yes = 100% of the answers.

**3b) Is HT officially accepted in your country by the national medical association?**

Yes = 100% of the answers.

**3c) Is HT a medical specialization\* in your country?**

Yes = 75% of the answers.

No = 25% of the answers.

\* this means it is practiced by specialized doctors after a post graduate specialization course.

**3d) Is HT included in other medical specializations in your country?**

Yes = 50% of the answers.

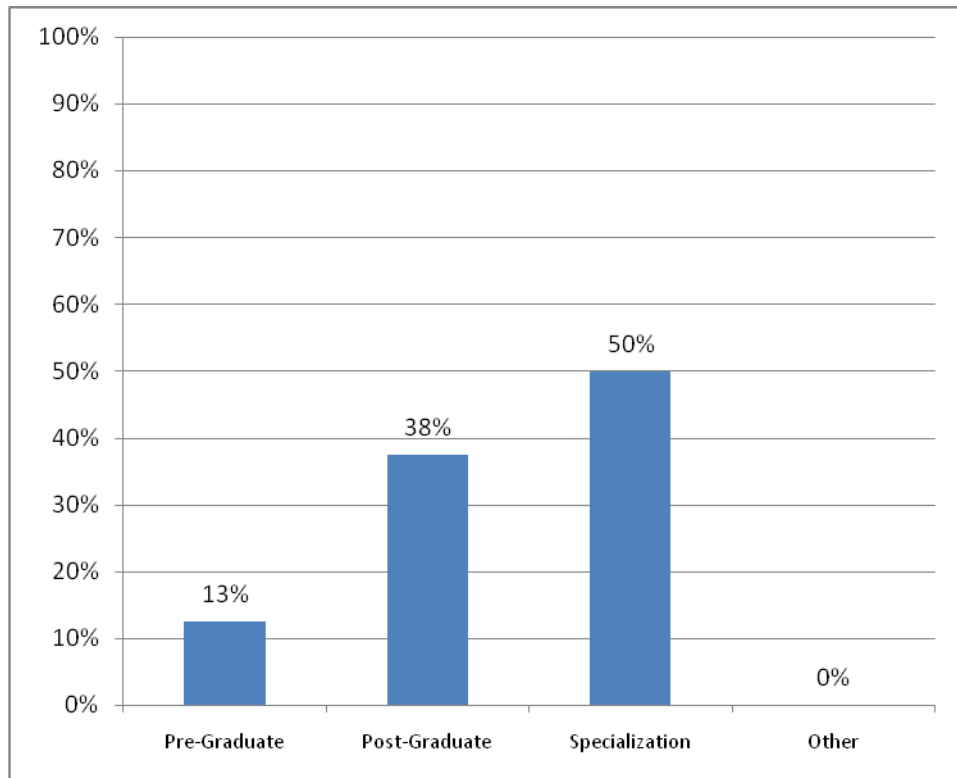
No = 50% of the answers.

**3e) Is there an HT medical education programme in your country?**

Yes = 87.5% of the answers.

No = 12.5% of the answers.

**3f) At what level(s) is training held?**

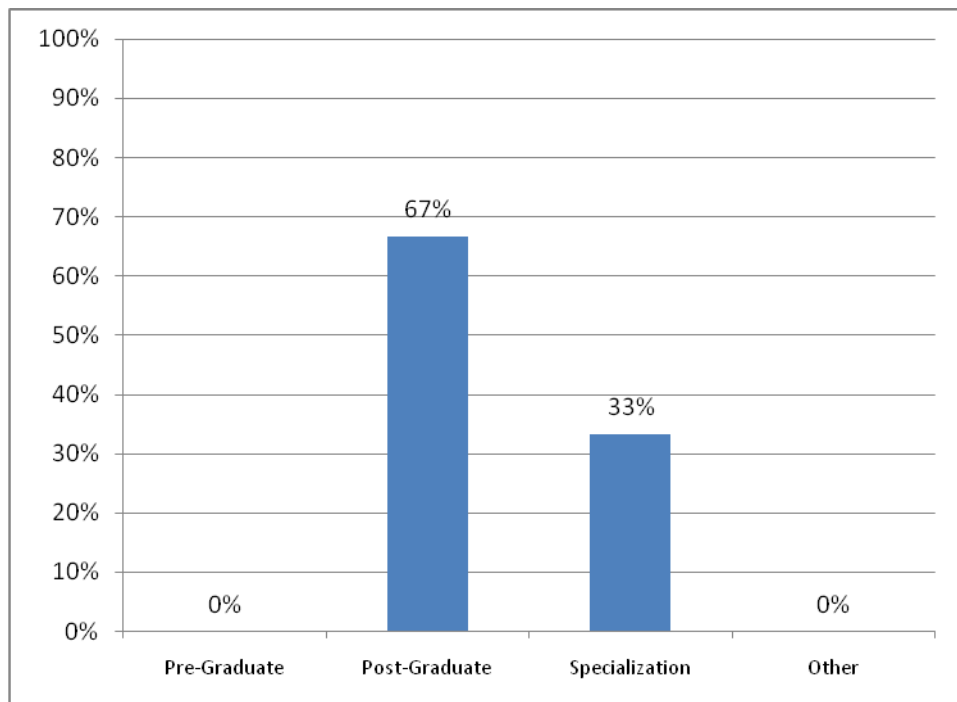


**3g) Is there any standardization for HT training programmes?**

Yes = 75% of the answers.

No = 25% of the answers.

**3h) At what levels of the HT programmes is the training standardized?**



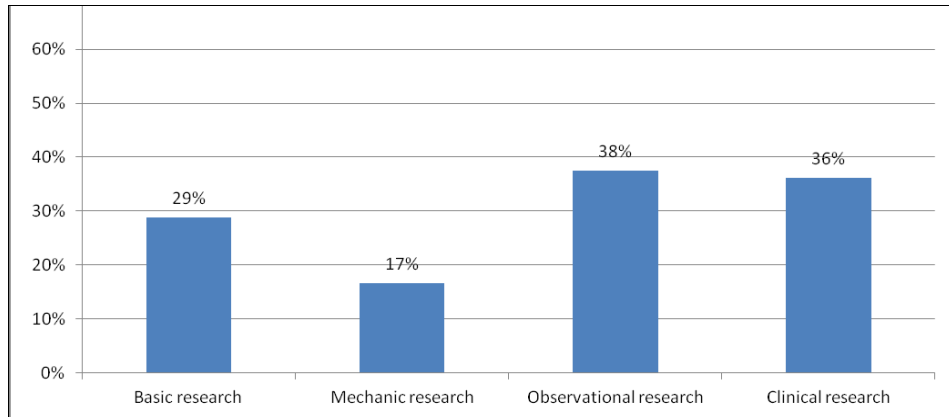
**3i) Do you think it would be beneficial to have standardization between training programmes in different countries where HT is practiced?**

Yes = 100% of the answers.

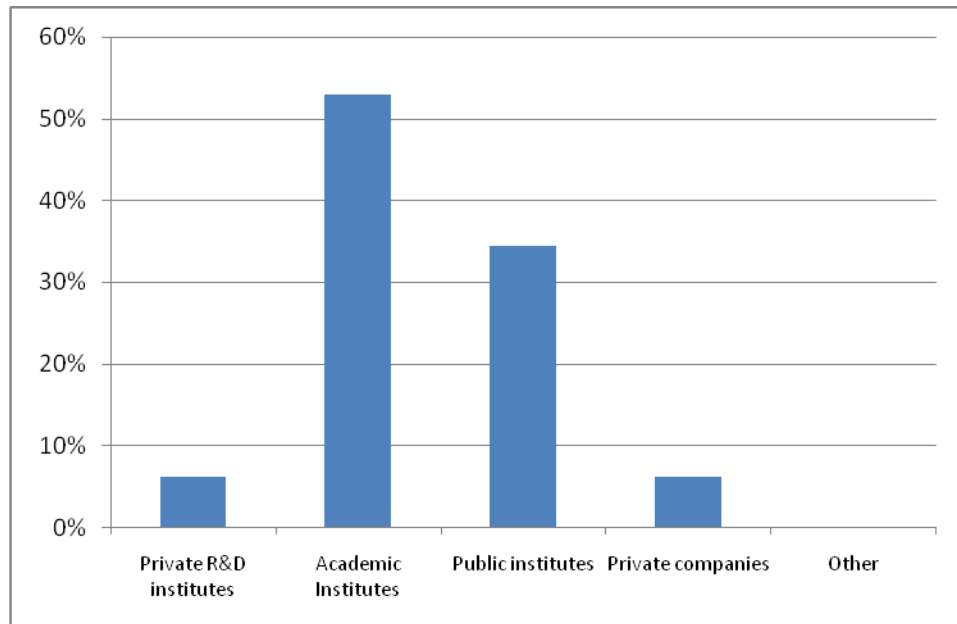
**3j) Do you think that a high-level training programme such as that used in many European countries could increase the quality, safety and efficacy of HT?**

Yes = 100% of the answers.

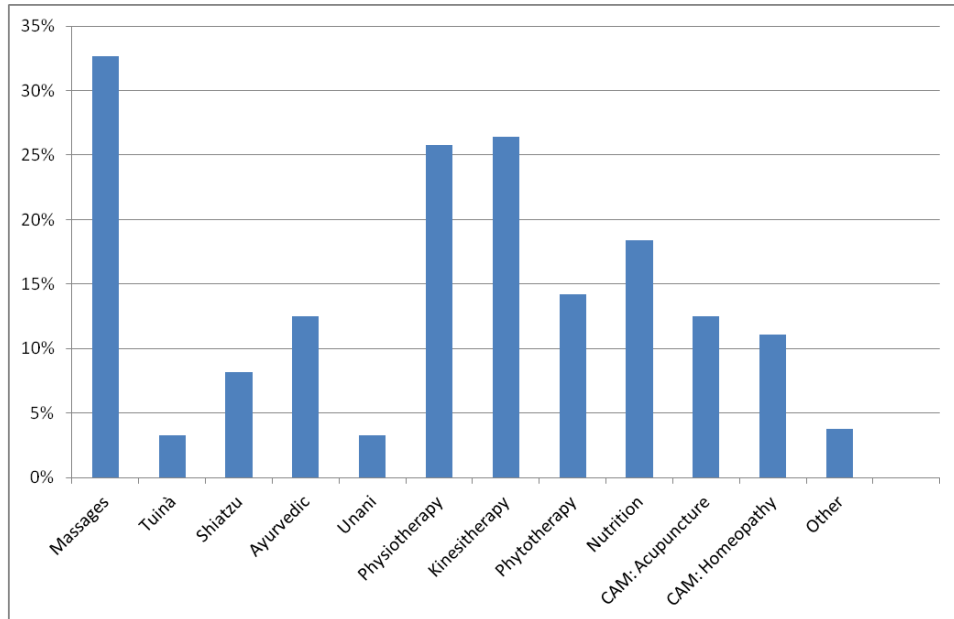
**3k) What is the most developed level of research?**



**3l) What types of institutes are most involved in research?**



**4) Please specify which of these therapies are most commonly used in thermal institutes in your country.**

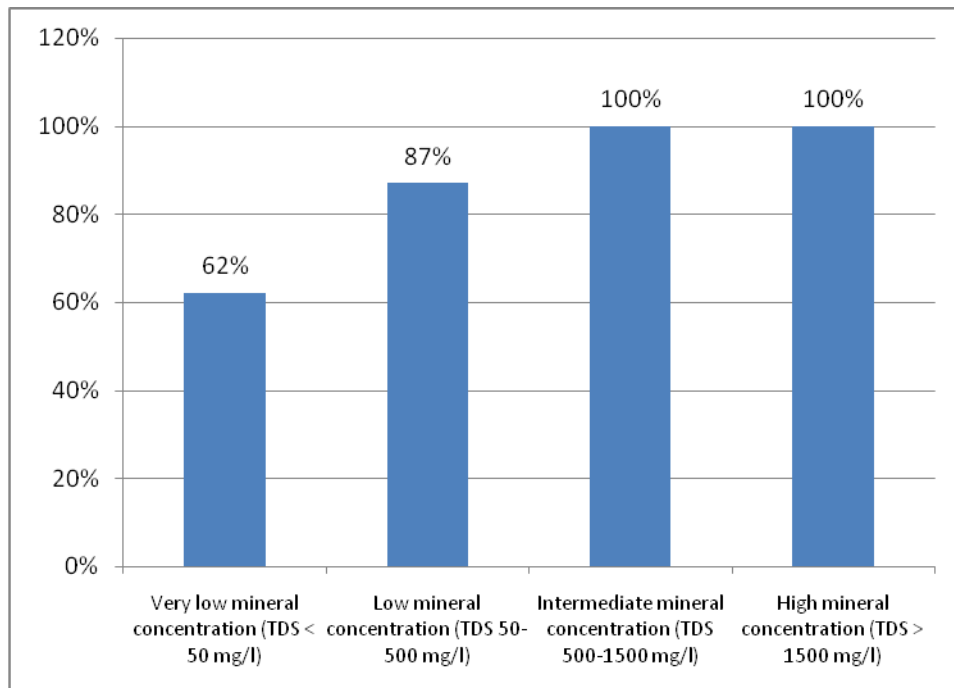


**4a) Are there any other types of public or private structures that use HT?**

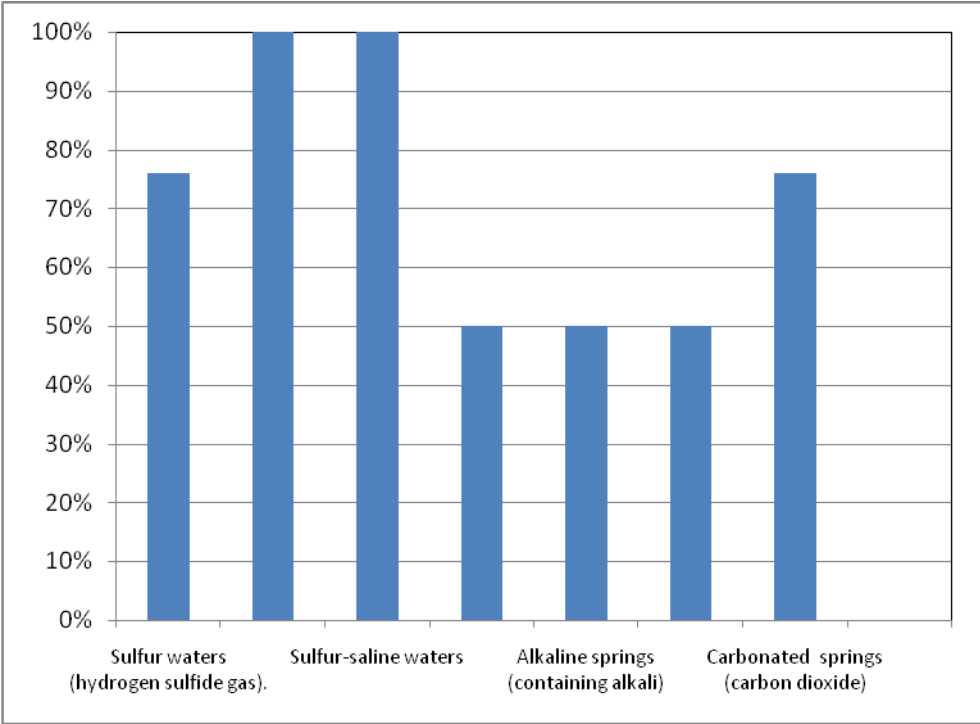
Yes = 75% of the answers.

No = 25% of the answers.

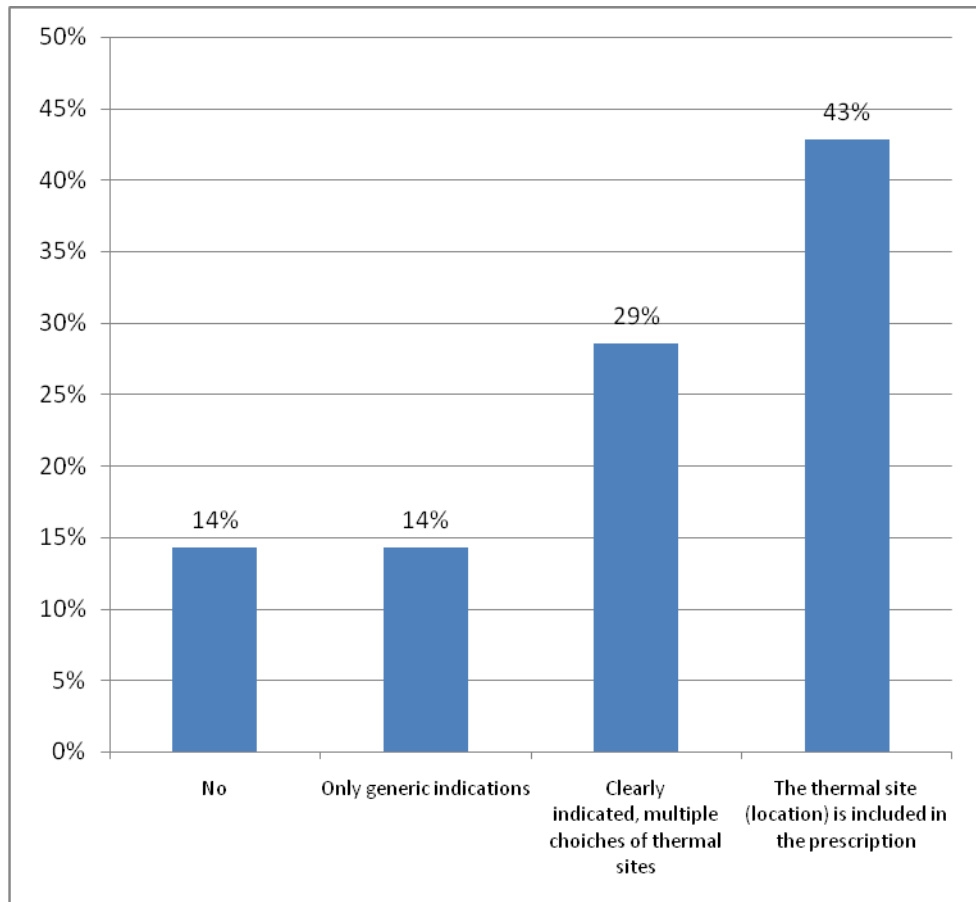
**4b) Which type of thermal water is used by the different HT structures?**



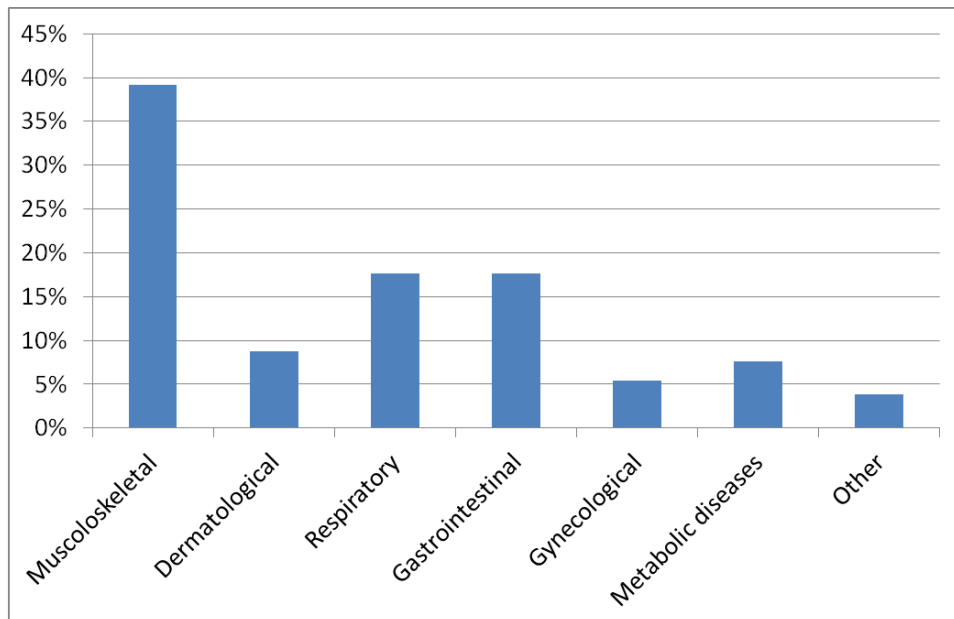
**4c) Which of the following characteristics of thermal waters are used by the different HT structures?**



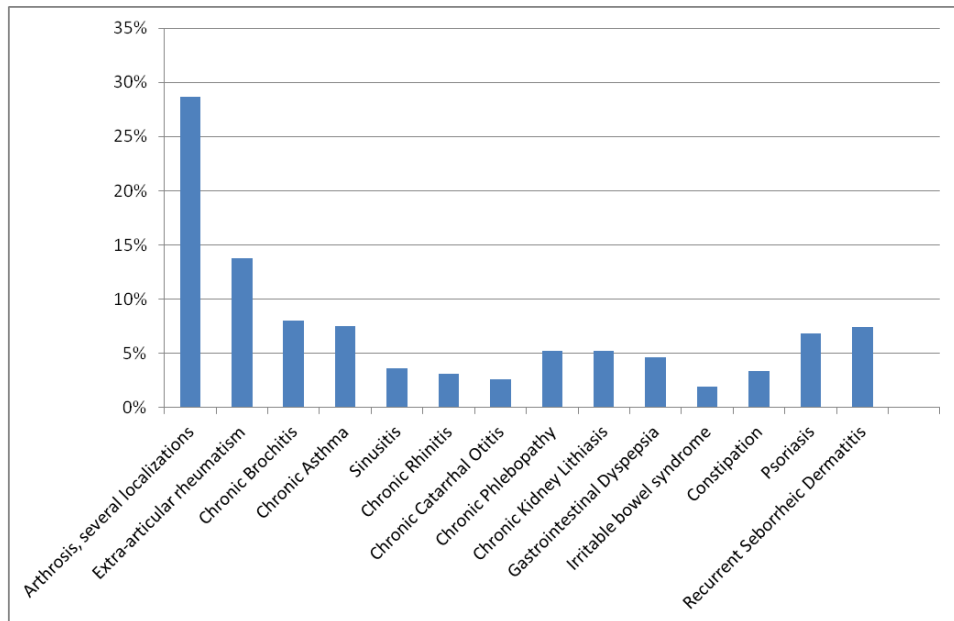
**4d) Whenever hydrological therapies are prescribed by a doctor, are the type and characteristics of the thermal waters clearly specified?**



**5) What are the fields in which HT is most commonly used in your country?**



**5a) What are the diseases for which HT is most commonly used? Please specify the percentage for each one.**



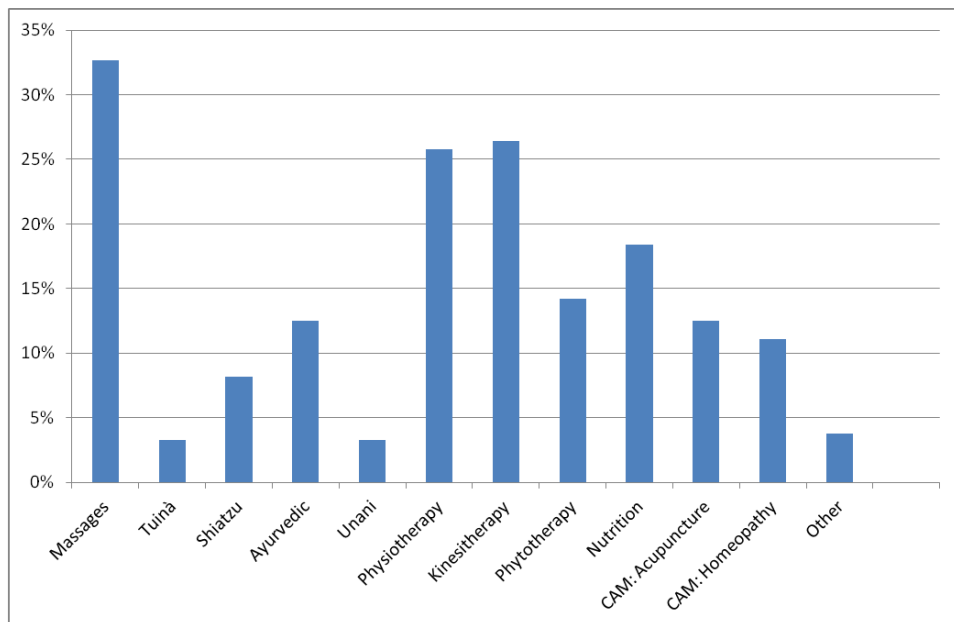
**5b) Please specify if the most diffused HT techniques in your country are used with specific and different indications for every disease?**

Yes = 100% of the answers.

**5c) Are any complementary medicine (CM) techniques used in your country as a complement to HT practices?**

Yes = 100% of the answers.

**5d) Please specify which and how common the following complementary medicine techniques are used together with HT?**



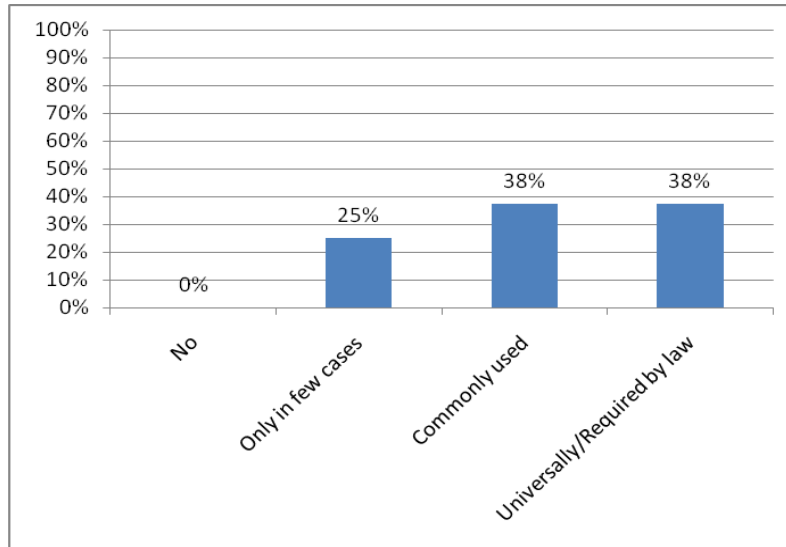


**5e) Have protocols for combining HT with other therapies been defined and used in your country?**

Yes = 25% of the answers.

No = 75% of the answers.

**5f) Is the administration of HT treatments registered in your country?**



**5g) Are possible side effects registered and tracked in your country?**

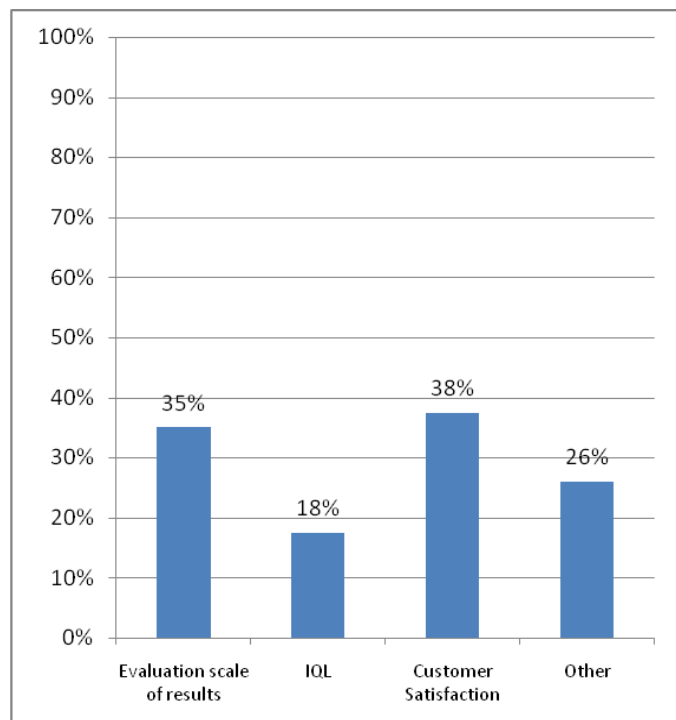
Yes = 50% of the answers.

No = 50% of the answers.

**5h) Does your country have evaluation systems in place to assess the results of HT treatments?**

Yes = 100% of the answers.

**5i) What system is generally used to evaluate the results of HT treatments? Please specify**



## LEGAL STATUS AND REGULATIONS ON HYDROTHERAPY

One of the key aspects of HT that this work has looked at is its legal status and the level of regulation present in the different countries that took part in the study. The legal status and regulations have been assessed via a specific questionnaire that is included below.

### TEXT OF HYDROTHERAPY LEGAL STATUS MONITORING SURVEY

Date:
Country:
Investigator's name:
Investigator's title:
Address:
Telephone:
Fax:
E-mail:

#### Introduction

With the widespread use of HT, the rapid expansion of international markets and people travelling, the development of national policies and regulations, HT has become an important issue for both health authorities and users. Providers of HT, other healthcare professionals and HT consumers alike are calling for regulations that can: ensure the safety of HT, promote the recognition of this system of therapy and further define its role in modern healthcare systems.

National policies and regulations on HT could ensure the safety, quality and efficacy of this system of therapy and be important steps towards integrative healthcare systems. However, relatively few countries have developed HT policies and regulations. Only very few countries and WHO members have a national HT policy.

With this survey, FEMTEC and FoRST are taking one step further towards an increased understanding of HT policies and regulations in several countries. By using a common approach to measuring the status of regulation in all countries, a comparative analysis of the results will be feasible and major themes and obstacles can be identified.

This survey is based on 15 qualitative and quantitative structural indicators designed to assess the status of HT policies and regulation. The

analysis of the survey results will provide the basis for further development of a comprehensive set of indicators.

## OBJECTIVES OF THIS SURVEY

The aim of this section of the study was to investigate the general legal framework for HT in the different countries that took part in the study, with the following objectives:

- To collect updated and comprehensive information on HT policies and regulations in several countries.
- To identify the specific needs of each country regarding capacity building for HT policies and regulation, which will enable WHO, on the basis of the study done by FEMTEC and FoRST to accordingly provide appropriate support to each specific countries.
- To monitor the impact of significant elements of the WHO strategy of TRM in relation to the rules, regulations and policies currently existing in the various countries. The aim is to collect specific data on different regulatory situations so as to encourage regulations in all countries. This activity is all the more important given consumer mobility. Today, consumers increasingly turn to professionals and facilities in other countries to find answers for their health and wellbeing needs. The international harmonization of rules is becoming increasingly important for HT too.

## FACT SHEET USED FOR THE LEGAL STATUS MONITORING SURVEY

### 1. Hydrotherapy (HT)

#### Useful explanations:

**Hydrotherapy (HT):** Traditional medicine is the sum total of knowledge, skills and practices based on the theories, beliefs and experiences indigenous to different cultures that are used to maintain health, as well as to prevent, diagnose, improve or treat physical and mental illnesses.

### Policy

#### Useful explanations:

**National HT policy:** A national HT policy could include some of the following key elements: a definition of HT, provision for the creation of laws and regulations, consideration of intellectual property rights, etc. The policy could further contain the main strategies proposed by the government for achieving the policy objectives.

**1. Is there a national HT policy? YES NO**

If **yes**, year of issue: \_\_\_\_\_

*Please submit a copy of the policy, if available in English, otherwise in the original language.*

If **no**, is such a policy in the process of being established? YES NO

**Law & Regulation**

**Useful explanations:**

**HT law:** A law is the first stage in the legislative procedure; it is a rule of conduct imposed by the authority. A law establishes the legal conditions under which HT should be organized in line with a national HT policy, or other relevant policies. The law could cover different areas in the HT field, for instance education of professionals, licensing of practitioners, etc. Both the public and private sectors could be taken into account.

**HT regulation:** Regulations form the second stage of legislative procedures, specifically designed to provide the legal machinery to achieve the administrative and technical goals of a law. Many activities in the field of HT could be covered by regulations, such as a description of obligations and responsibilities of licensed practitioners, the penal sanctions if these are not respected, etc.

**2. Is there a national law or regulation on HT? YES NO**

If **yes**, year of issue: \_\_\_\_\_

*Please submit a copy of the law and/or regulation, if available in English, otherwise in the original language.*

If **no**, is such a law or regulation in the process of being established? YES NO

**National Programme**

**Useful explanations:**

**National HT programme:** A national HT programme is defined here as any programme performed at local or national level, by the ministry of health, by other ministries, or by local bodies, whose mandate is to take concrete action in order to achieve objectives in line with the national policy or legislation.

**3. Is there a national HT programme? YES NO**

If **yes**, year of issue: \_\_\_\_\_

*Please submit a copy of the description of the programme, if available in English, otherwise in the original language.*

If **no**, is such a programme in the process of being established? YES NO

**National Office**

**4. Is there a HT national office? YES NO**

If **yes**, year of establishment: \_\_\_\_\_

*Please provide the contact address for the national office.*

**Under which Ministry is it administered?**

Ministry of Health

Other, namely \_\_\_\_\_

If **no**, is the establishment of such an office planned? YES NO

**Expert Committee**

**Is there an expert committee for HT? YES NO**

If **yes**, year of establishment: \_\_\_\_\_

*Please provide the contact address to the expert committee.*

<p><b>National Research Institute</b></p> <p><b>Useful explanations:</b></p> <p><i>A national HT research institute is a research institute that performs HT research and is fully or partially funded by the government.</i></p>
---

**6. Is there a national research institute for:**

**YEAR OF ESTABLISHMENT**

HT? YES NO \_\_\_\_\_

**7. What is the regulatory status of HT?**

**Please tick everything that applies.**

Prescription therapies

Self-therapy only

Therapy in a separate regulatory category

Other, namely

No status

**Claims**

**Useful explanations:**

**Medical claims:** Medical claims are defined here as those claims specified to treat, cure or prevent a disease or restore, correct or modify physiological functions.

**Health claims:** Health claims are defined here as follows: “any statement, suggestion or implication in labelling or advertising that a product carries a specific health benefit, but not nutritional claims nor medicinal claims. The term health claim further includes claims that refer to nutrient function and recommended dietary practice”.

**Structure/function claims:** These claims link a substance to an effect on a structure or function of the body

**8. Is HT used with claims in your country? YES NO**

If **yes**, by law/regulation, what type of claims are made for HT?

	<b>Please tick everything that applies.</b>
Medical claims	
Health claims	
Structure/function claims	
No claims can be made according to the law	
Other claims, namely	

**Safety**

**9a. What are the regulatory requirements for HT safety assessments?**

**Please tick everything that applies.**

Same requirements as for conventional therapies

Special requirements, namely

Traditional use without demonstrated harmful effects

Reference to documented scientific research

Other requirements, namely \_\_\_\_\_

No requirements

**Comments:**

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**9b. Does any control mechanism ensure the implementation of the safety requirements for HT? YES NO**

If **yes**, please explain the type of control mechanism used.

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**Essential Drug List**

**10. Are hydrotherapies included in the national essential drug list? YES NO**

**Post-marketing Surveillance**

**11. Is there a post-marketing surveillance system for hydrotherapies? YES NO**

If **yes**, is there a national system to monitor the adverse effects of hydrotherapies? YES NO

**Year of establishment:** \_\_\_\_\_

If **no**, are there any plans to establish such a system? YES NO

**Market**

**12.5. How are hydrotherapies provided?**

	<b>Please tick everything that applies.</b>
In clinics as prescription therapies	<input type="checkbox"/>
In hydrotherapy institutes	<input type="checkbox"/>
In spas	<input type="checkbox"/>
By licensed practitioners	<input type="checkbox"/>
No restrictions for providing hydrotherapies	<input type="checkbox"/>
Other ways, namely	<input type="checkbox"/>

**13. The countries, WHO and HT**

**Useful explanations:**

WHO wants to learn more about the needs of each Member State, so the feedback from each country is an essential part of WHO providing countries with useful help in the future.

**14. What are the main difficulties faced by your country as regards HT regulatory issues?**

Lack of research data	<input type="checkbox"/>
Lack of expertise within the national health authorities and control agency	<input type="checkbox"/>
Lack of appropriate mechanisms for the control of hydrotherapy	<input type="checkbox"/>
Lack of education and training	<input type="checkbox"/>
Other, namely	<input type="checkbox"/>

**15. What kind of support on HT related topics would your country like to receive from WHO?**

	Please tick options as prioritized.		
	MUCH NEEDED	NEEDED	NOT NEEDED
Information sharing on regulatory issues			
Training workshops about national capacity to establish hydrotherapy regulations			
General guidelines for hydrotherapy research and evaluation			
Training workshops about national capacity building on hydrotherapy safety monitoring			
Provision of databases			
Organization of global meetings			
Other, namely			

#### 16. How would you like WHO to present the results from this survey?

As a descriptive report

As a condensed report with results presented in figures/tables

Results/analysis presented in a database

#### PARTICIPANTS

The experts who took part in the survey are from various countries and are the people indicated below:

- **China** Cao Wen Fu
- **Cuba** Florana Menéndez Camporredondo
- **France** Christian-François Roques Latrille
- **Hungary** Thamas Bender
- **Italy** Antonella Fioravanti
- **Poland** Irena Ponikowska
- **Portugal** Pedro Cantista
- **Romania** Olga Surdu, MD, PhD
- **Russian Federation** Nikolay Storozhenko; Igor Bobrovinski
- **Tunisia** Taoufik Khalfallah

#### CONCLUSIONS

In general, looking at the answers provided by the different countries, it is possible state that three groups of legislation, regulation and education have emerged from the answers provided by the different countries.

The first is represented by the European countries and it includes both the Western and Eastern European countries. The use of HT is highly regulated. In these countries, training of professionals is generally at university level, with postgraduate specialization.

The second situation is found in countries like Tunisia and other North African countries, which have a long-standing HT tradition. These



countries are starting to pass HT rules and regulations quite swiftly, especially following strong local demand and the protection mechanisms that consequently need to be put in place.

Finally, there is a third situation, in countries like China, where the regulatory level is still in the early stages, although things are moving. Often, in these countries HT is used for fun, or to relax and there is no medical side to the treatment.

## GENERAL SUMMARY AND DISCUSSION

### CONTEXT

HT is the use of the water in different physical conditions and chemical compositions with many methodologies - both traditional and scientific - to treat and prevent health problems as well as to keep people healthy.

HT can be classified under the label of traditional medicine (TRM) as clearly specified in WHO's "*General Guidelines for Methodologies on Research and Evaluation of Traditional Medicine*" Geneva WHO/EDM/TRM/2000.1, p. 985

However, in some countries it could also be classified under complementary and alternative medicines (CAM).<sup>86</sup>

The FEMTEC and FORST Committing Committee asked a Committee of Experts from several countries to describe the current situation with a view to disseminating knowledge of these therapies, exploring or reviewing the scientific evidence on which such therapy is based and implementing the laws and regulations present in some countries, but not in all.

The Committing Committee requested WHO support to ensure the safe, efficacious and proper use of these therapies and to facilitate the uniformity of laws and regulations adopted by different countries in order to protect consumers all over the world.<sup>87,88</sup>

### OBJECTIVES AND METHODS

The report aims to respond to the following questions:

- How can thermal therapy be defined, and how is it used by the population?

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<sup>85</sup> 2.1 Types of traditional procedure-based therapies

Traditional procedure-based therapies are therapies that use various techniques, primarily without the use of medication, to provide healthcare. They include, for example, acupuncture and related techniques, chiropractic, osteopathy, manual therapies, qigong, tai chi, yoga, naturopathy, thermal medicine, and other physical, mental, spiritual and mind-body therapies.

<sup>86</sup>In 2007 the National Center for Complementary and Alternative Medicine (NCCAM) of the National Institute of Health (US) defined these medicines as a "group of diverse medical and healthcare systems, practices and products that are not currently considered to be part of conventional medicine". These therapies are referred to as 'complementary' when they are used jointly with conventional treatments, and as "alternative" when they are used instead of conventional treatment.

<sup>87</sup> WHO, *WHO-TRM Strategy 2002-2005*, WHO Geneva, 2002, WHO/EDM/TRM/2002.1

<sup>88</sup>WHO, *Guidelines on Developing Consumer Information on Proper Use of Traditional, Complementary and Alternative Medicine*, WHO Geneva, 2004

- How effective is HT? What are the benefits and the potential adverse reactions?
- What is the legal status of these medicines and how are they organized in countries around the world?
- How are therapists trained?
- To ensure a complete understanding of these therapies, given their complex and multidimensional nature, a range of methods were used:
  - medical literature was analysed to assess the clinical effectiveness and safety of the therapies being studied;
  - a survey of the general population gave a view of the scale of use of such therapies;
  - an online survey among practitioners provided a description of their characteristics and those of their practices;
  - a detailed analysis of the legal and organizational regulatory framework helped to understand the normative level of these therapies in several countries;
  - a consultation with the professional associations and experts gave insight into how these professions are organized and how their practitioners are trained.

Together they draw a picture of the current state in some countries, but they cannot provide a complete answer to the initial research questions because of the limitations of each method and the resulting limitations of the material collected.

To create this general overview, we triangulated the results of the different studies.

## **LIMITATIONS**

Despite the range of methods that were used, this study has some limitations. The key ones are listed below.

- The literature search was potentially limited to a review of reviews, i.e. excluding findings from more recent primary studies. The quality of the reviews was variable, but above all, the studies included in the reviews were predominantly low quality and little safety information was found. Given the focus on systematic reviews, the literature study is biased towards subjects or studies for which systematic reviews were published.
- The sociological part is exploratory, and the practitioners' survey focuses on a small purposive sample of specialists who are likely to already believe in the value of the therapy. As such, this group is not representative of the entire group of practitioners, and certainly not representative of the whole population of practitioners. Although the

survey covers a broader range of countries than in the past, it still remains a small sample. The findings could nevertheless shed light on the results of the population survey and give indications about the perception of acupuncture and the way consultations take place.

- Likewise, the therapists who agreed to an interview may not be representative of all therapists.

Who are the participants?

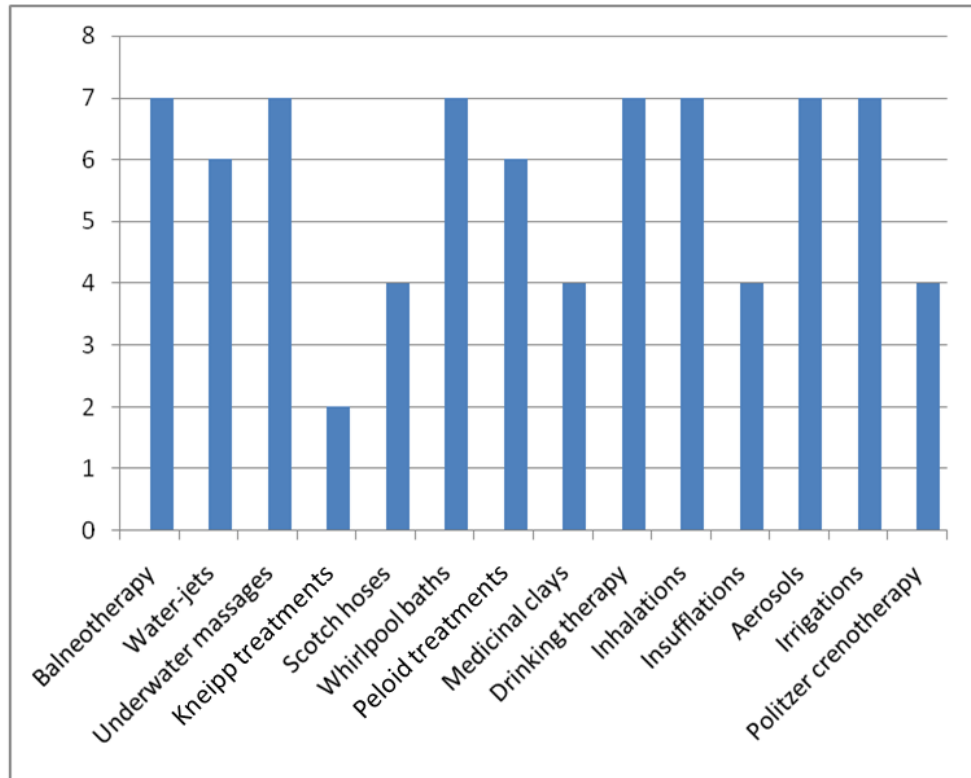
- **China:** Cao Wen Fu
- **Cuba:** Florana Menéndez Camporredondo
- **France:** Christian-François Roques Latrille
- **Hungary:** Thamas Bender
- **Italy:** Antonella Fioravanti
- **Poland:** Irena Ponikowska
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- **Romania:** Olga Surdu, MD, PhD
- **Russian Federation:** Nikolay Storozhenko  
- Igor Bobrovinski
- **Tunisia:** Taoufik Khalfallah

In every state, each expert identified the centres of reference for HT treatment. Then, a multiple-choice questionnaire was submitted to each expert. The answers to the questionnaire were sent to the Committed Committee. In order to have an initial understanding of the situation with HT in the various countries involved in the monitoring survey, the Committed Committee processed the results statistically.

**SCHEME FOR INVESTIGATING THE MONITORING SURVEY AND COMMENTS ON THE ANSWERS**

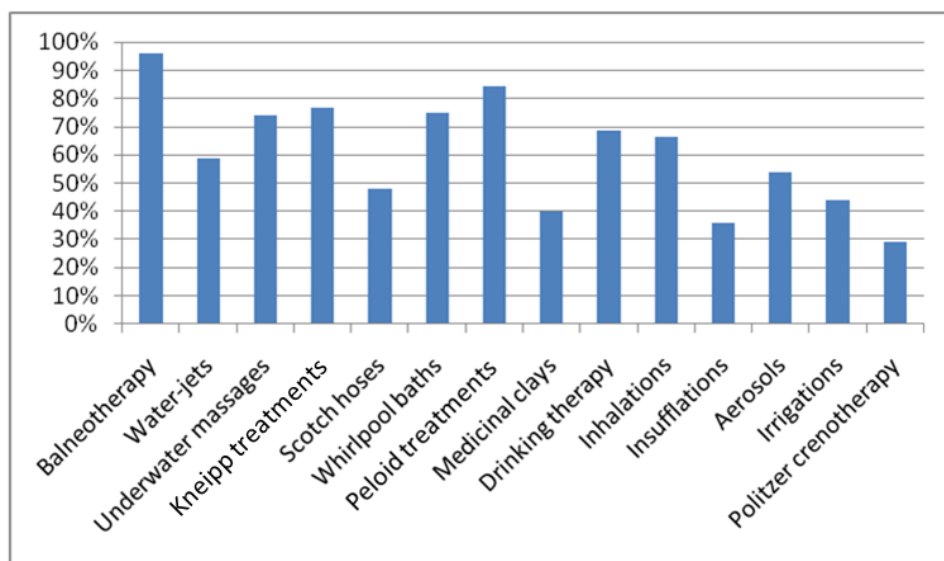
The section below highlights the key questions by commenting on the answers.

**1A) What types of HT practices are there?**



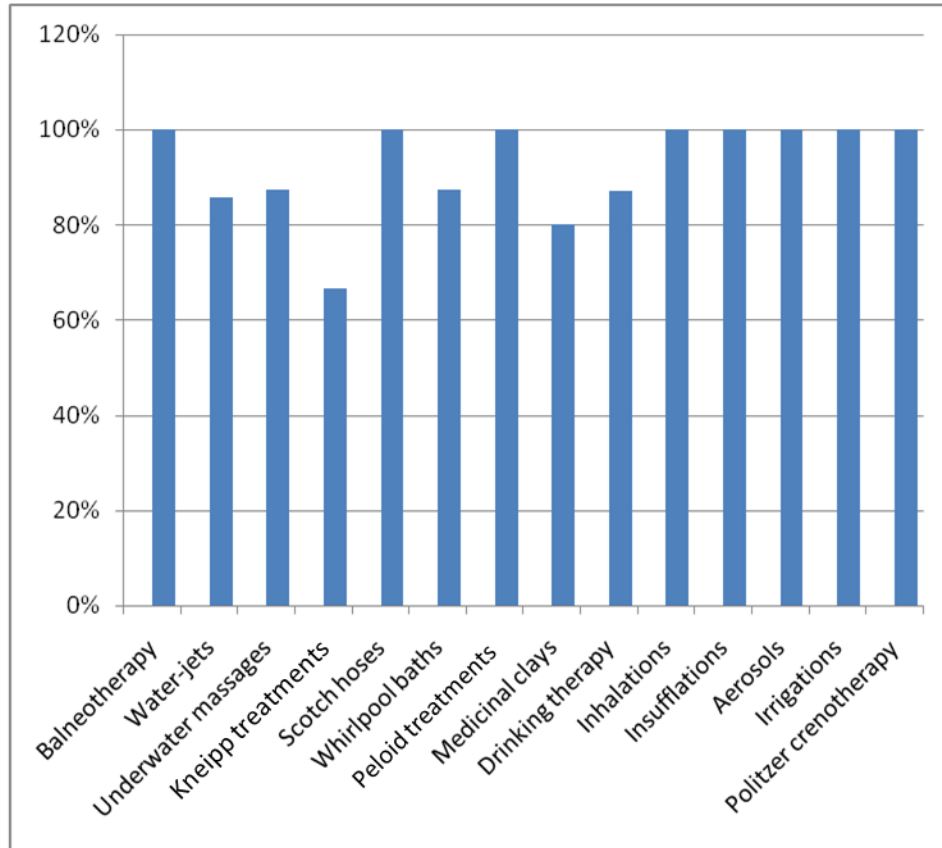
In this section we have analysed various centres around the world to identify the services provided by HT centres, such as spas or clinics.

**1B) Which is the most frequently used?**



From the data it appears that balneotherapy and peloid treatments are the most commonly used for osteo-joint and muscle disease, playing an important role in the treatment of chronic pain. Between HT baths is an important time for vascular diseases according to the Kneipp method. HT is frequently applied with inhalation treatments and drinking therapies for respiratory and digestive tract cures, respectively.

1C) Which of these therapies are subject to medical prescriptions?

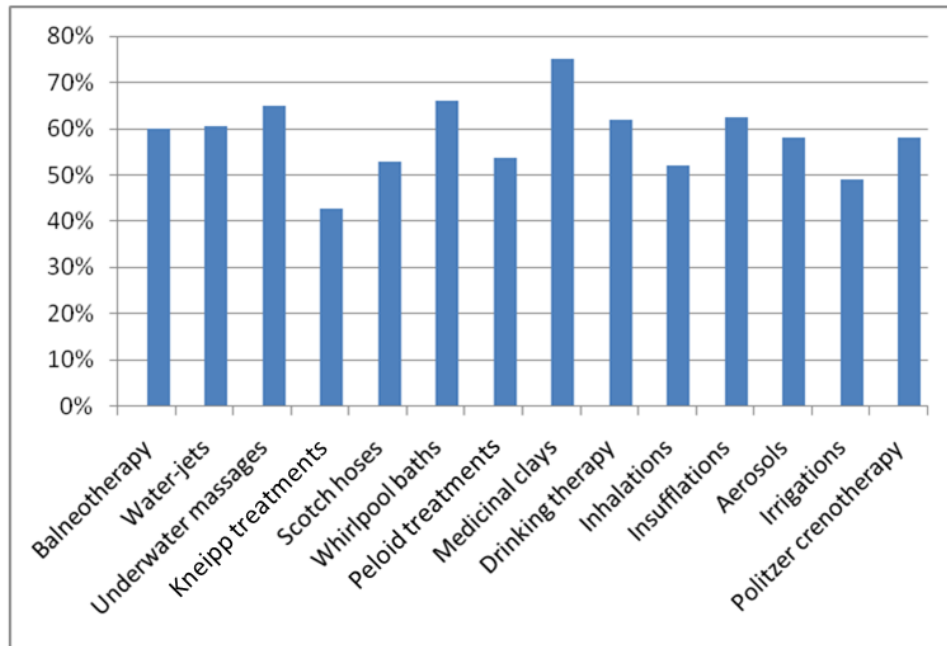


Possible answers:

- Balneotherapy/ water jets/ underwater massage / Kneipp treatments/ Scotch hose / whirlpool bath/ peloid/ medicinal clay;
- Drinking therapy;
- Inhalation/ insufflation/ aerosol;
- Irrigation;
- Politzer crenotherapy.

As we can see from the answers (from the various reference people in the different countries), most therapies are prescribed by a doctor. Even in cases where a prescription is not mandatory (e.g. Kneipp treatments and whirlpool baths), in most cases, there is a general assessment by a doctor of the patient.

1D) Which of these therapies are provided under doctor supervision?



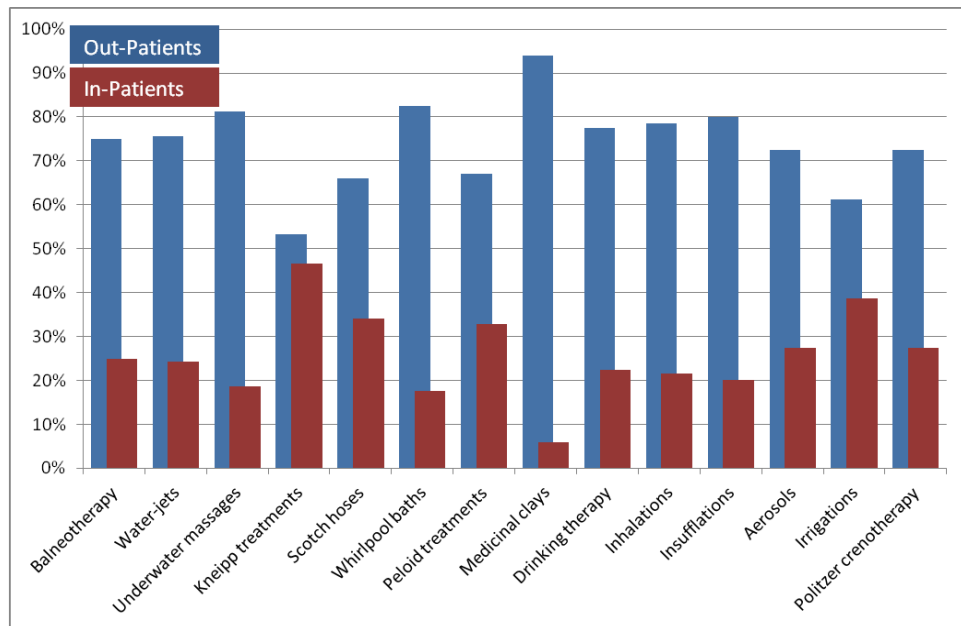
*Possible answers:*

- Balneotherapy/ water jets/ underwater massage / Kneipp treatments/ Scotch hose / whirlpool bath/ peloid/ medicinal clay;
- Drinking therapy;
- Inhalation/ insufflation/ aerosol;
- Irrigation;
- Politzer crenotherapy.

In general, it can be said that in most of the centres - but not in those countries where thermal medicine has developed more recently - there is supervision by a physician to assess the general and specific suitability of the patient to have the treatments. However, the presence of a doctor is not always required for the application of a single therapy, unless it becomes necessary for the application of specific therapies.

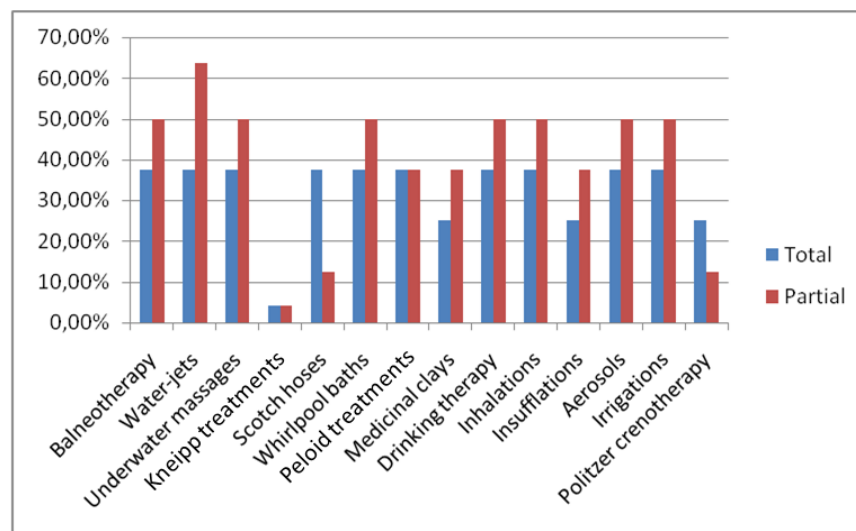
An example of this is Politzer crenotherapy, which is performed by a doctor, who is often an ENT specialist because of the delicate, specific nature of the treatment. In centres where complementary therapies have been introduced to support classical HT - such as, acupuncture, herbal medicine, mesotherapy, and so on - applications are only done under medical supervision.

1F) Which of these therapies are used on out-patients and which on in-patients?



In many countries, especially, in eastern Europe, there are some facilities, either hotel-like or clinic-like, where patients can receive HT treatments while being hospitalized or in a residential format, following traditionally accepted models and protocols. Certainly, such an approach to HT forces patients to comply strictly to resting and reaction times, which, in HT and thermal settings, are key to fully benefitting from these treatments. These aspects also ensure more accurate applications of treatments. As can be inferred from the chart, most treatments are out-patient, however it is interesting to note that there is a small percentage of cases in which treatments are provided in a residential/hospitalization mode.

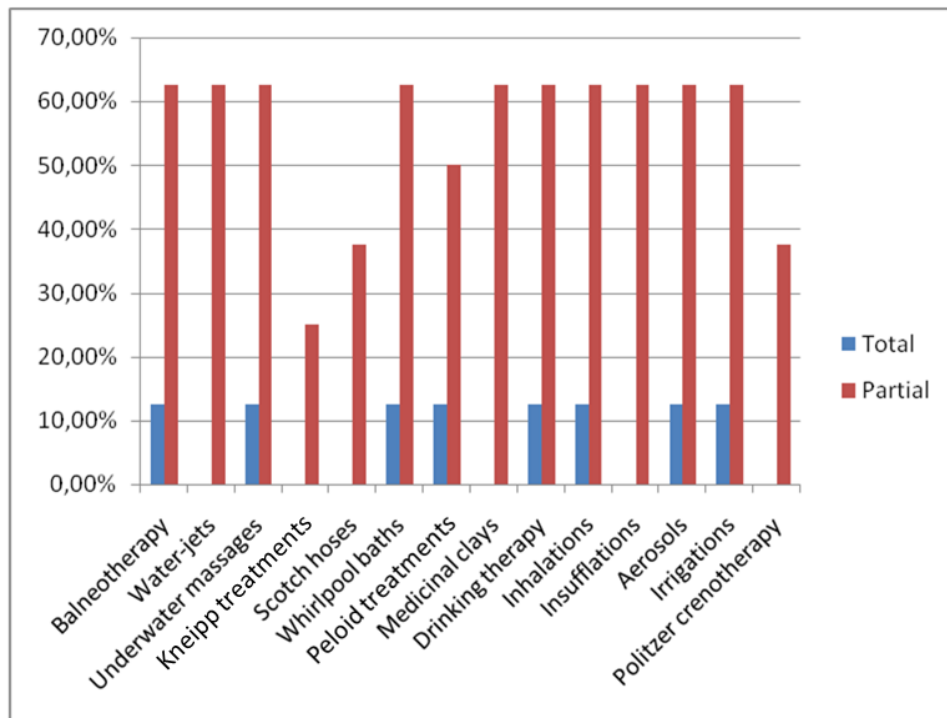
2B) Is there official reimbursement for all or part of these therapies from the public authorities?





The chart clearly shows that basically no country provides full coverage, but, as often happens, the state provides partial coverage. This is interesting, especially because it is reasonable to assume that the state keeps paying for some types of treatment that it assumes are somehow effective or that it believes prevents other problems. In countries where the state does not provide any coverage, there still are some private insurance options for reimbursing the costs (see next chart). However, state and private insurance reimbursements are increasingly tied to evidentiary proof of the efficacy of the treatment. Thus, from this point of view, the hope is that there will be an increase not only in efficacy studies, but also in cost/benefit analyses that can make it easier for regulatory authorities to decide whether to reimburse or not these treatments.

2C) Is there official reimbursement of all or part of these therapies by private insurance firms?



**3) Is HT "membership" officially accepted in your country by the scientific medical community?**

In all states the response was 100%

**3A/3B) Is HT officially accepted in your country by the scientific academic community (Universities)? Is HT considered a medical specialty in your country? (This means that is practiced by specialized doctors, after a specialist post graduate course).**

The answer to the first question was 100%. In terms of the second question, only 75% of participating states have post-graduate specialization courses for graduate doctors.

**3E) In your country is there any HT medical education programme?**

The response was affirmative for 87.5%.

**3F) At what level(s) is training held?**

- Pre-graduate: 12.5%;
- Post graduate: 37.5;
- Specialization 50%.

**3G) Is there any standardization for HT training programmes?**

The answer was affirmative for 75%.

**3H) At what levels of the HT programmes is the training standardized?**

- post graduate: 66.67%
- specialization: 33.33%

**3I) Do you think it would be beneficial to have standardization between training programmes in different countries where HT is practiced?**

The answer was unanimous (100%)

**3J/3K) Would it be useful to have some form of standardization of training programmes in the various countries in which HT is practiced and do you believe that a high-level training programme, such as that used in many European countries, could help to ensure the quality, safety and effectiveness of HT?**

The answer was unanimous (100%). None of the participants was able to tell which programme was the best.

Regarding the type of HT research, the reference people in the different countries contacted believe the following are the most developed: observational research 3.75%; clinical research: 3.62%; basic research: 2.88% and mechanical research: 2.62.

**3l) What types of institutes are most involved in research?**

- private R&D institutes: 1.75%;
- academic institutes 3.62%;
- public institutes 2.88;
- private companies: 1.75%;
- others: 1%.

The answers to this set of questions show that in most countries, HT has generally good medical support, which means it is accepted, at different levels, by almost all parts of the national healthcare system.

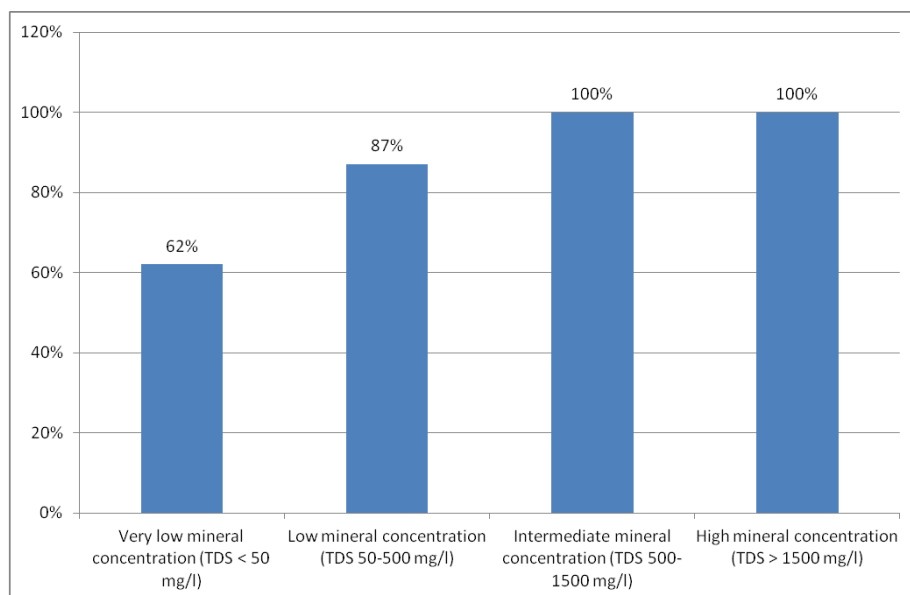
As such, although research in this field is not that common, it is done with fairly good methods by physicians and a general focus on clinical aspects, even though there is some basic research. It is also worth noting that the organizations that do research in this field are mainly public bodies or universities, accounting for roughly double the number of private organizations that do research in this field.

#### 4) How many SPA institutes are there in your country?

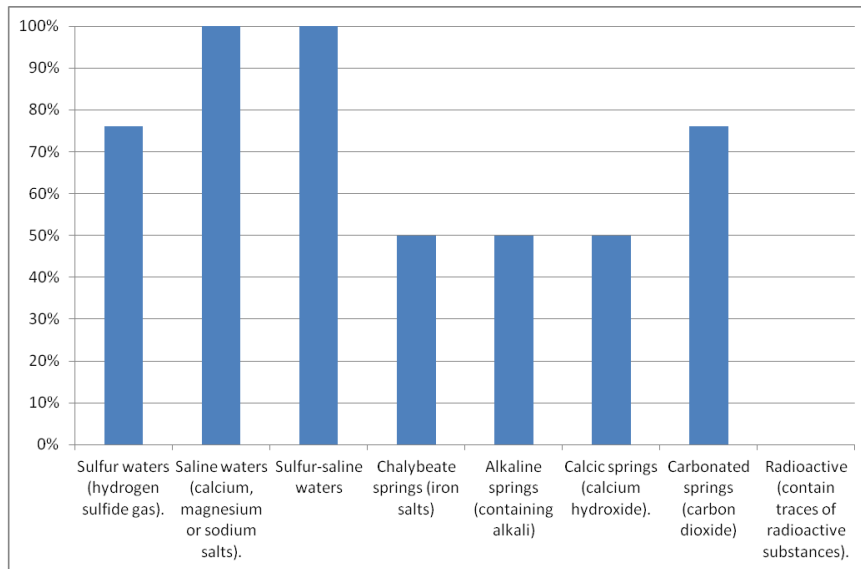
- China ~300
- Cuba ~30
- France ~250
- Hungary ~120
- Italy ~400
- Poland ~120
- Portugal ~50
- Romania ~130
- Russia ~1300
- Tunisia ~70

This question enabled the team to assess the presence of HT centres, even non-thermal ones. For some time now, alongside specific thermal services, HT practices that also focus on prevention and improving wellbeing (rather than providing specific cures) have been on the market.

#### 4C) What type of thermal water is used in the different HT structures?

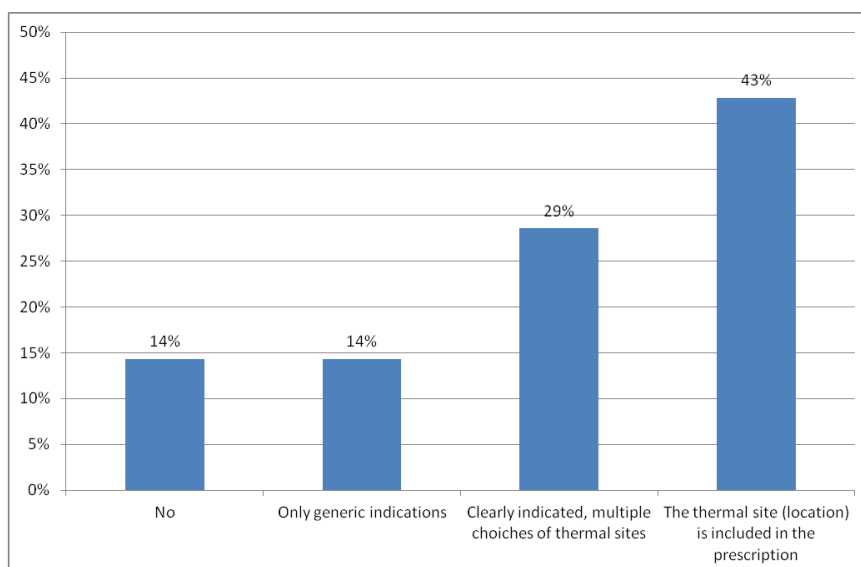


**4D) Which of the following characteristics of thermal waters are used by the different HT structures?**

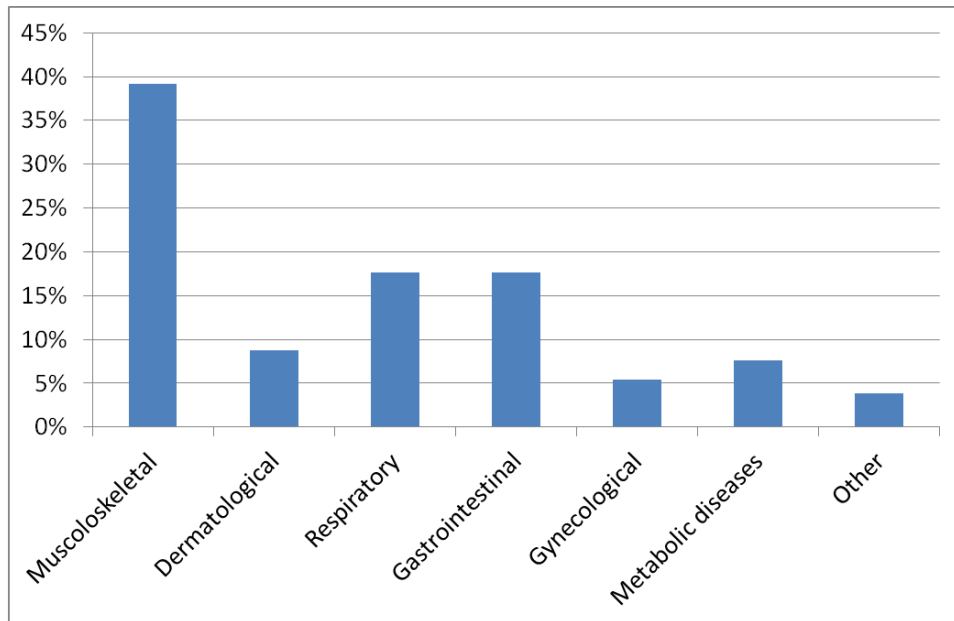


The previous question and the following ones up to 5A clearly show a certain level of specialization, especially with crenotherapy, given the ability to identify the various chemical components of mineral water and the indications of use, which depend on the specific effect of the minerals in the water. This is one sphere where traditional HT knowledge is being enriched by new research and it is clear that the traditional knowledge has pretty close links to the data coming from new scientific research. Going ahead, it will be interesting to observe to what extent scientific documentation will be able to support this traditional use of mineral water.

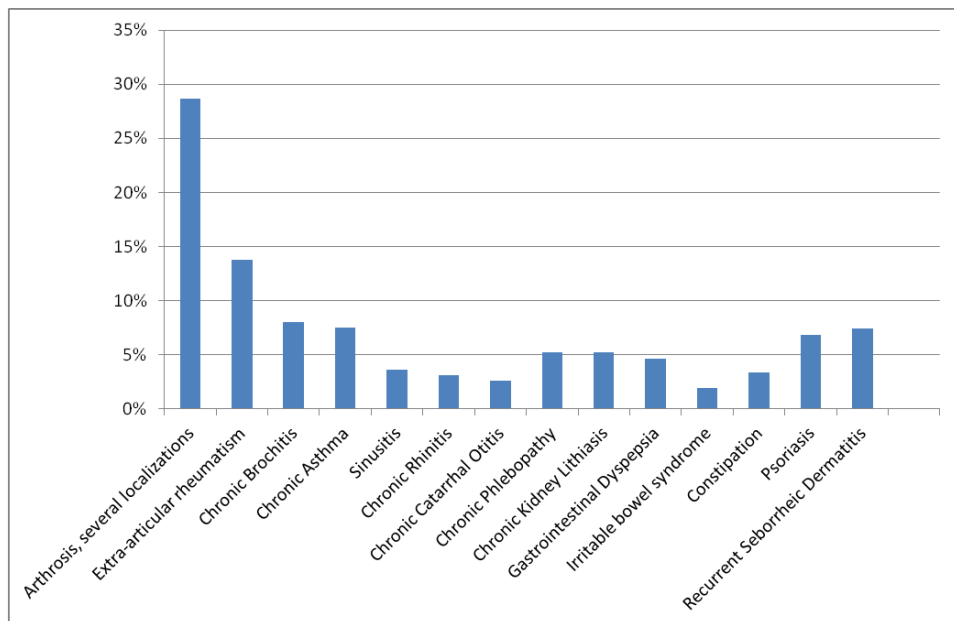
**4E) Whenever hydrological therapies are prescribed by a doctor, are the type and characteristics of the thermal waters clearly specified?**



**5) What are the fields in which HT is most commonly used in your country?**



**5A) What are the most common fields in which HT is used?**

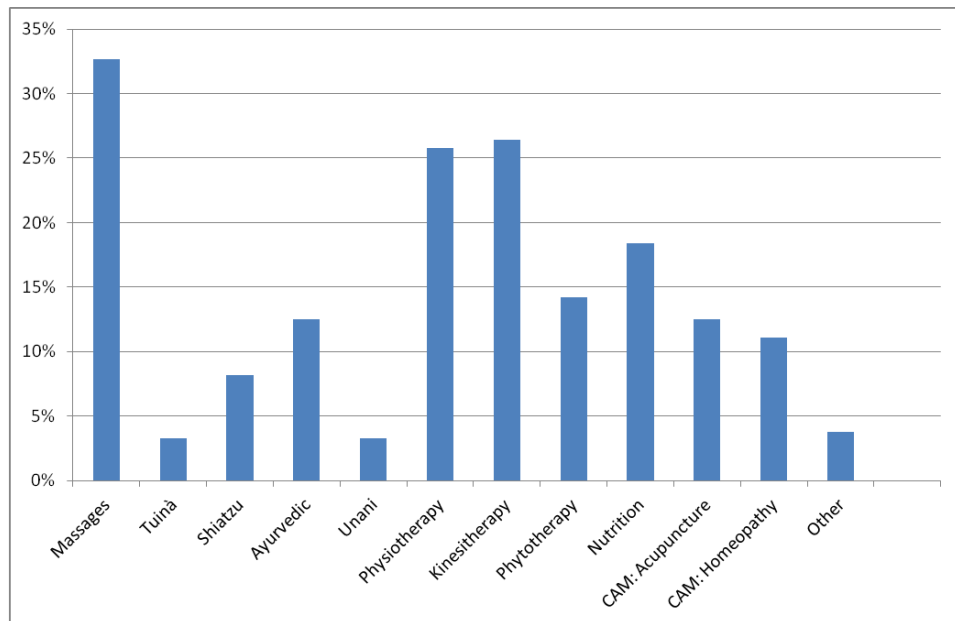


**5B) Could you specify whether the most common HT techniques in your country are used in conjunction with specific and different techniques for each disease?**

Yes.

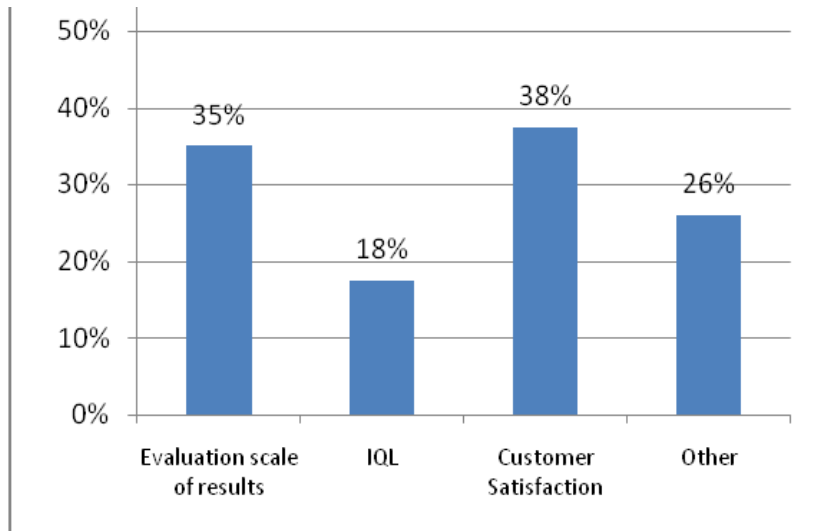
**5C) Are any complementary medicine (CM) techniques used in your country as a complement to HT practices?**

Yes.



The two previous questions show a relatively new phenomenon that can be noted in many HT centres, namely, combining HT with other traditional and complementary medicine techniques. Massage practices, like Tui Na or Ayurveda, acupuncture and phytotherapy are increasingly used in HT centres across the world. The reasons for such mixing is linked to consumers who are looking for a wide array of natural therapies, which include thermal treatments and complementary medicine. The picture is interesting and extremely promising, even though it poses some issues in terms of efficacy, safety, quality, and definition of protocols. All of this still needs to be defined. In this context, it is interesting to note how active and spontaneous the HT world in China has been in systematically combining HT and traditional drugs in the treatment of rheumatic conditions.

**5I) What system is generally used to evaluate the results of HT treatments? Please specify**



This last question is designed to assess to what extent and how HT practices are systematically assessed during everyday use. The results show that HT is a practice that is routinely monitored - especially in terms of its effects - using assessment scales that are quite weak but simple and very common. Indirectly, we can infer from this information that the thermal environment could potentially be a place to be used for doing research, something that, thus far, has not been done as well as it could have been.

## CONCLUSIONS

From the study on the use and the diffusion of HT we can say that the countries studied can be divided into three groups.

- In the first group HT is widely used by the population. The therapies and practices are often included in the national healthcare system. This group includes most European countries, along with the Russian Federation.
- In the second group, HT is used as complementary medicine. These therapies are often provided at spas or in other locations. In most of these countries, there is no reimbursement for people who use such treatments.
- There is also a third group, in which the population is more and more oriented towards the use of HT, but in these countries HT is not seen as part of the healthcare system or as complementary medicine. HT is merely used for leisure and wellness purposes.
- Regarding the legislative regulatory framework in relation to the situation and education in various countries we can once again divide the countries into three groups:
- There is a group that includes both the Western and Eastern European countries that have high levels of government regulation and legislation for the use of HT. In these countries, academic training of practitioners is mostly at university level with the presence of post-graduate training programmes and improvements of genuine specialization schools.
- There are also countries, such as in North Africa (Tunisia, Morocco and Algeria), which is an area with great HT traditions, where HT is in the process of being legislated and regulated, especially as consumers are seeking as much and people need to be safeguarded.
- The same situation can be found in Latin American countries, with the exception of Cuba. In Cuba, HT is recognized by the Ministry of Health and by the national health system.
- Finally, there are countries such as Japan, South Korea, Vietnam and China where, despite the great historical tradition, HT is an innovative methodology that at the moment is not always included between complementary and traditional medicine.



- The analysis of studies used for this work shows quite a mixed bag. There were meta analyses, systematic reviews, controlled randomized trials, observational studies and research on action mechanisms.

The fields where most information was retrieved are also quite different: orthopaedics, cardiovascular and respiratory systems, dermatology. Several of the studies used had small patient populations, and their outcome measures were heterogeneous. The studies are often very different and not homogenous in terms of type, intensity, and duration of treatment. In terms of the methodology and clinical assessments, the difference is significant. Moreover, the selection of a suitable control group may be difficult, and the construction of a blind model is often impossible. The older studies are of poor quality, but in the last 10 years, the design and implementation of RCTs conforms to generally accepted guidelines.

In general it can be said that the evidence for the treatment of musculoskeletal disease is more solid, while for other areas, research methodology is often poor, recruitment unsatisfactory and study design is faulty.

The cause for such poor evidence to support HT is probably ascribable to its ancient origins. It started and developed during historical times when scientific methods were unknown. Scientific assessment is relatively new for HT.

So, tradition would indicate it is best to maintain the uses and applications that are so popular and requested by people. Nonetheless, it is fundamental to develop more in-depth systematic research methods to ensure safety and more adequate use, thus safeguarding users.

## BIBLIOGRAPHICAL REFERENCES

- Agostini G., *Manuale di Medicina Termale*, Archimedita, Turin 2000
- Arnould-Taylor W., *Princípios e prática de fisioterapia*. ed. Artmed, Porto Alegre 1999
- Boron W., Boulpeap E., *Medical Physiology*, Saunders/Elsevier, Philadelphia 2009
- Broglio A., Colucci V., *Riabilitazione in acqua*, Edi Ermes, Milan 2001
- Buchman D.D., *Terapia pela água: 500 maneiras de usar a mais antiga das medicinas naturais*, Brasiliense, Sao Paulo 1981
- Campion M.R., *Hidroterapia: princípios e práticas*, Manole, São Paulo 2000
- Messini M., *Trattato di idroclimatologia clinica I*, Cappelli Editore, Bologna 1950
- Grossior A., Held J.P., *Kinébalnothérapie, médecine de rééducation*, Flammarion edit. Paris 1981
- Solimene U., Bruttomesso G., *Medicina termale*, Red Edizioni, Milan 2010
- WHO, *Guidelines on Developing Consumer Information on Proper Use of Traditional, Complementary and Alternative Medicine*, WHO Geneva, 2004, available online at: <http://apps.who.int/medicinedocs/en/d/Js5525e/> visited on 14 May 2013
- WHO, *WHO-TRM Strategy 2002-2005*, WHO Geneva, 2002, WHO/EDM/TRM/2002.1, available on line at: <http://apps.who.int/medicinedocs/en/d/Js2297e/> visited on 14 May 2013
- WHO, *General Guidelines for Methodologies on Research and Evaluation of Traditional Medicine*, available online at: [http://whqlibdoc.who.int/hq/2000/WHO\\_EDM\\_TRM\\_2000.1.pdf](http://whqlibdoc.who.int/hq/2000/WHO_EDM_TRM_2000.1.pdf), visited on 14 may 2013

## ON-LINE REFERENCES

- Anales de Hidrologia Medica*, Spagna, Universidad Complutense de Madrid, [www.ucm.es/info/hidromed](http://www.ucm.es/info/hidromed)
- Balneo Research Journal*, Romania, *Editura Balneara*, <http://bioclima.ro/Journal.htm>
- Balneologia-Gyógyfürd ügy-Gyógyidegenforgalom*, Ungaria, Magyar Balneológiai Egyesület Minden jog fenntartva, [www.balneologia.hu](http://www.balneologia.hu)
- Balneology - Journal of ISMH*, Turchia, International Society of Medical Hydrology and Climatology, <http://www.ismh-direct.net/info.aspx?sp=4>
- China Hot Spring Tourism Association*, China, Femtec China, <http://www.hstcn.com/>; [http://femteconline.org/index.php?option=com\\_content&view=category&id=66&Itemid=144](http://femteconline.org/index.php?option=com_content&view=category&id=66&Itemid=144)
- Journal of Rehabilitation Medicine*, Russia, [www.rj-rm.ru](http://www.rj-rm.ru)
- La Presse Thermale et Climatique*, Francia, La Société française de médecine thermale, [www.socmedthermale.org/la-presse-thermale-et-climatique](http://www.socmedthermale.org/la-presse-thermale-et-climatique)
- Office National du Thermalisme et de l'Hydrothérapie*, Tunisia, <http://hydrotherapie.openvision-tn.com/index.php?id=23&L=0>
- Polish Association of Balneology and Physical Medicine*, Polonia, [www.balneologia.pl](http://www.balneologia.pl)
- Revue médicale suisse*, Svizzera, Groupe Médecine & Hygiène, [www.medhyg.ch/revue medicale suisse](http://www.medhyg.ch/revue_medicale_suisse)
- The Journal of the Japanese Society of Balneology, Climatology and Physical Medicine*, Giappone, <http://www.journalarchive.jst.go.jp>

# Annex A

## CARDIOVASCULAR SYSTEM

### Paper 1

Circ J. 2010 Apr;74(4):617-21. Epub 2010 Feb 13.

#### **Waon therapy for cardiovascular disease: innovative therapy for the 21st century.**

Miyata M, Tei C.

#### **Source**

Department of Cardiovascular, Respiratory and Metabolic Medicine, Graduate School of Medicine, Kagoshima University, Kagoshima, Japan. miyatam@m3.kufm.kagoshima-u.ac.jp

#### **Abstract**

Waon therapy is a form of thermal treatment in a dry sauna maintained at a temperature of 60 degrees C, which differs from the traditional sauna. Waon therapy reportedly improves the hemodynamics, cardiac function, ventricular arrhythmias, vascular endothelial function, neurohormonal factors, sympathetic nervous system function, and symptoms in patients with chronic heart failure (CHF). It has also been demonstrated that the molecular mechanism by which Waon therapy improves vascular flow and endothelial function involves increased expression of endothelial nitric oxide synthase (eNOS). Furthermore, in a mouse model of hindlimb ischemia, repeated Waon therapy increased eNOS protein expression, blood flow, and capillary density. Moreover, Waon therapy did not increase blood flow and capillary density in eNOS-deficient mice, indicating that eNOS is a critical regulator of the angiogenesis induced by this therapy. Moreover, repeated Waon therapy is effective for patients with severe peripheral arterial disease (PAD), as evidenced by substantial decrease in pain scores, increases in both ankle-brachial pressure index and blood flow assessed by laser Doppler perfusion imaging, and by formation of new collateral vessels on angiography. In addition, ischemic ulcers heal or improve markedly. In conclusion, Waon therapy is an innovative and highly promising strategy for treating CHF and PAD.

PMID: 20154403 [PubMed - indexed for MEDLINE] [Free full text](#)

### Paper 2

J Cardiol. 2008 Oct;52(2):79-85. Epub 2008 Aug 27.

#### **Beneficial effects of Waon therapy on patients with chronic heart failure: results of a prospective multicenter study.**

Miyata M, Kihara T, Kubozono T, Ikeda Y, Shinsato T, Izumi T, Matsuzaki M, Yamaguchi T, Kasanuki H, Daida H, Nagayama M, Nishigami K, Hirata K, Kihara K, Tei C.

#### **Source**

Department of Cardiovascular, Respiratory and Metabolic Medicine, Graduated School of Medicine, Kagoshima University, 8-35-1 Sakuragaoka, Kagoshima 890-8520, Japan. miyatam@m3.kufm.kagoshima-u.ac.jp

## **Abstract**

### **BACKGROUND:**

We conducted a prospective multicenter case-control study to confirm the clinical efficacy and safety of Waon therapy on chronic heart failure (CHF).

### **METHODS:**

Patients (n=188) with CHF were treated with standard therapy for at least 1 week, and then were randomized to Waon therapy (n=112) or a control group (n=76). All patients continued conventional treatment for an additional 2 weeks. The Waon therapy group was treated daily with a far infrared-ray dry sauna at 60 degrees C for 15 min and then kept on bed rest with a blanket for 30 min for 2 weeks. Chest radiography, echocardiography, and plasma levels of brain natriuretic peptide (BNP) were measured before and 2 weeks after treatment.

### **RESULTS:**

NYHA functional class significantly decreased after 2 weeks of treatment in both groups. Chest radiography also showed a significant decrease of the cardiothoracic ratio in both groups (Waon therapy: 57.2+/-8.0% to 55.2+/-8.0%, p<0.0001; control: 57.0+/-7.7% to 56.0+/-7.1%, p<0.05). Echocardiography demonstrated that left ventricular diastolic dimension (LVDd), left atrial dimension (LAD), and ejection fraction (EF) significantly improved in the Waon therapy group (LVDd: 60.6+/-7.6 to 59.1+/-8.4 mm, p<0.0001; LAD: 45.4+/-9.3 mm to 44.1+/-9.4 mm, p<0.05; EF: 31.6+/-10.4% to 34.6+/-10.6%, p<0.0001), but not in the control group (LVDd: 58.4+/-10.3 mm to 57.9+/-10.4 mm; LAD: 46.3+/-9.7 mm to 46.2+/-10.1 mm; EF: 36.6+/-14.1% to 37.3+/-14.0%). The plasma concentration of BNP significantly decreased with Waon therapy, but not in the control group (Waon: 542+/-508 pg/ml to 394+/-410 pg/ml, p<0.001; control: 440+/-377 pg/ml to 358+/-382 pg/ml).

### **CONCLUSION:**

Waon therapy is safe, improves clinical symptoms and cardiac function, and decreases cardiac size in CHF patients. Waon therapy is an innovative and promising therapy for patients with CHF.

PMID: 18922381 [PubMed - indexed for MEDLINE]

## **Paper 3**

J Cardiol. 2011 Jan;57(1):100-6. Epub 2010 Sep 29.

### **Improvement of autonomic nervous activity by Waon therapy in patients with chronic heart failure.**

Kuwahata S, Miyata M, Fujita S, Kubozono T, Shinsato T, Ikeda Y, Hamasaki S, Kuwaki T, Tei C.

### **Source**

Department of Cardiovascular, Respiratory and Metabolic Medicine, Graduate School of Medicine, Kagoshima University, Kagoshima 890-8520, Japan.

## **Abstract**

### **BACKGROUND AND PURPOSE:**

We have reported previously that Waon therapy improves cardiac and vascular function, and prognosis of patients with chronic heart failure (CHF). CHF is characterized by generalized sympathetic activation and parasympathetic withdrawal. The purpose of this study was to evaluate the effect of Waon therapy on autonomic nervous activity in patients with CHF.

## **METHODS AND SUBJECTS:**

Fifty-four patients with CHF, who were receiving conventional therapy for CHF, were divided into Waon therapy and control groups. In the Waon therapy group, 27 patients were treated with medication and Waon therapy. In the control group, 27 patients were treated with only conventional CHF therapy. Cardiac function including cardiac output (CO) and left ventricular ejection fraction (LVEF) was evaluated by echocardiography. The heart rate variability, such as the coefficient of variation of RR intervals (CVRR), the low-frequency (LF) component, high-frequency (HF) component, the LF norm [LF/(LF+HF)], and HF norm [HF/(LF+HF)], were measured at admission and 4 weeks after treatment.

## **RESULTS:**

Echocardiography demonstrated that CO and LVEF significantly increased after 4 weeks in the Waon therapy group, but did not change in the control group. In the Waon therapy group, CVRR, HF, and HF norm significantly increased 4 weeks after Waon therapy. In addition, the LF/HF ratio and LF norm significantly decreased 4 weeks after Waon therapy. In contrast, these parameters remained unchanged in the control group. Moreover, the HF and HF norm were significantly higher, and the LF/HF ratio and LF norm were significantly lower after 4 weeks of Waon therapy group than after 4 weeks of only conventional therapy.

## **CONCLUSIONS:**

Waon therapy improved cardiac function and autonomic nervous activity by increasing parasympathetic and decreasing sympathetic nervous activity in patients with CHF.

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PMID: 20884178 [PubMed - indexed for MEDLINE]

## **Paper 4**

J Cardiol. 2009 Apr;53(2):214-8. Epub 2009 Jan 18.

## **Waon therapy improves the prognosis of patients with chronic heart failure.**

Kihara T, Miyata M, Fukudome T, Ikeda Y, Shinsato T, Kubozono T, Fujita S, Kuwahata S, Hamasaki S, Torii H, Lee S, Toda H, Tei C.

## **Source**

Department of Cardiovascular, Respiratory and Metabolic Medicine, Graduate School of Medicine, Kagoshima University, 8-35-1 Sakuragaoka, Kagoshima 890-8520, Japan.

## **Abstract**

### **BACKGROUND:**

We developed a Waon therapy (soothing warm therapy) and have previously reported that repeated Waon therapy improves hemodynamics, peripheral vascular function, arrhythmias, and clinical symptoms in patients with chronic

heart failure (CHF). The aim of this study was to investigate the effect of Waon therapy on the prognosis of CHF patients.

### **PATIENTS AND METHODS:**

We studied 129 patients with CHF in NYHA functional class III or IV who were admitted to our hospital between January 1999 and March 2001. In the Waon therapy group, 64 patients were treated with a far infrared-ray dry sauna at 60 degrees C for 15 min and then kept on bed rest with a blanket for 30 min. The patients were treated daily for 5 days during admission, and then at least twice a week after discharge. In the control group, 65 patients, matched for age, gender, and NYHA functional class, were treated with traditional CHF therapy. The follow-up time was scheduled for 5 years.

### **RESULTS:**

Recent, complete follow-up data on each patient were obtained. The overall survival rate was 84.5% (Kaplan-Meier estimate). Twelve patients died in the control group and 8 patients died in the Waon therapy group at 60 months of follow-up. Cardiac events due to heart failure or cardiac death occurred in 68.7% of the control group but only 31.3% of the Waon therapy group ( $P<0.01$ ) at 60 months of follow-up.

### **CONCLUSION:**

Waon therapy reduced cardiac events in patients with CHF. This therapy is a promising non-pharmacological treatment for CHF.  
PMID: 19304125 [PubMed - indexed for MEDLINE]

## **Paper 5**

Circ J. 2011;75(2):348-56. Epub 2010 Dec 14.

### **Effect of Waon therapy on oxidative stress in chronic heart failure.**

Fujita S, Ikeda Y, Miyata M, Shinsato T, Kubozono T, Kuwahata S, Hamada N, Miyauchi T, Yamaguchi T, Torii H, Hamasaki S, Tei C.

### **Source**

Department of Cardiovascular, Respiratory and Metabolic Medicine, Graduate School of Medicine, Kagoshima University, Kagoshima, Japan.

### **Abstract**

#### **BACKGROUND:**

A previous report by our team showed that Waon therapy, using a far infrared-ray dry sauna at 60°C, improves cardiac and vascular function in patients with chronic heart failure (CHF). The purpose of the present study was to clarify the effect of Waon therapy on oxidative stress in CHF patients and investigate its mechanism by animal experiments.

#### **METHODS AND RESULTS:**

Forty patients with CHF were divided into control (n=20) and Waon therapy (n=20) groups. All patients received standard optimal medications for CHF. Waon therapy group was treated with Waon therapy daily for 4 weeks. After 4 weeks of Waon therapy, concentrations of hydroperoxide and brain natriuretic peptide (BNP) decreased significantly (hydroperoxide, 422±116 to 327±88U.CARR,  $P<0.001$ ; BNP, 402±221 to 225±137pg/ml,  $P<0.001$ ), and the

nitric oxide metabolites increased ( $71.2 \pm 35.4$  to  $92.0 \pm 40.5$  mmol/L,  $P < 0.05$ ). In contrast, none of these variables changed over the 4-week interval in the control group. Furthermore, animal experiments were performed using TO-2 cardiomyopathic hamsters. On immunohistochemistry, cardiac expression of 4-hydroxy-2-nonenal, a marker of oxidative stress, was decreased in the 4-week Waon therapy compared to untreated hamsters. On Western blotting, cardiac expressions of heat shock protein (HSP) 27, manganese superoxide dismutase and HSP32, which reduce oxidative stress, were significantly upregulated in the 4-week Waon therapy compared to untreated hamsters.

## CONCLUSIONS:

Waon therapy decreases oxidative stress in patients and hamsters with heart failure.

PMID: 21173495 [PubMed - indexed for MEDLINE] [Free full text](#)

## Paper 6

J Cardiol. 2010 Nov;56(3):361-6. Epub 2010 Sep 16.

## Waon therapy mobilizes CD34+ cells and improves peripheral arterial disease.

Shinsato T, Miyata M, Kubozono T, Ikeda Y, Fujita S, Kuwahata S, Akasaki Y, Hamasaki S, Fujiwara H, Tei C.

## Source

Department of Cardiovascular, Respiratory and Metabolic Medicine, Graduate School of Medicine, Kagoshima University, 8-35-1 Sakuragaoka, Kagoshima 890-8520, Japan.

## Abstract

### BACKGROUND:

We previously reported that Waon therapy upregulates endothelial nitric oxide synthase protein, and augments ischemia-induced angiogenesis in mice with hindlimb ischemia, and it improves limb ischemia in patients with peripheral arterial disease (PAD). The aim of this study was to investigate the underlying mechanism of Waon therapy for the treatment of patients with PAD, and to determine whether Waon therapy can mobilize blood-derived progenitor cells.

### METHODS:

21 consecutive PAD patients received standard medications, and were randomly divided into control ( $n=10$ ) and Waon therapy groups ( $n=11$ ). The Waon therapy group received Waon therapy daily for 6 weeks. The control group continued conventional therapy for 6 weeks. Leg pain was scored using a visual analogue scale. The ankle-brachial pressure index (ABPI) and the 6-min walking distance were measured at baseline and 6 weeks after therapy. Frequency of circulating CD34+ progenitor cell numbers was measured by quantitative real-time polymerase chain reaction, and the serum nitrate and nitrite levels were also measured at baseline and 6 weeks after therapy.

### RESULTS:

The leg pain score, ABPI and the 6-min walking distance improved significantly after 6 weeks in the Waon therapy group, but not in the control group. Frequency of circulating CD34+ cells increased after 6 weeks of Waon therapy [ $2.0 \pm 1.2$  ( $\times 10^{-4}$ ) at baseline to  $3.9 \pm 1.9$  ( $\times 10^{-4}$ ),  $p=0.015$ ], while it remained unchanged in the control group [ $1.8 \pm 1.8$  ( $\times 10^{-4}$ ) at baseline to  $1.2 \pm 0.9$

( $\times 10^{-4}$ )). Serum nitrate and nitrite levels increased significantly after Waon therapy ( $29.6 \pm 17.6$  to  $36.0 \pm 17.7$   $\mu\text{mol/ml}$ ,  $p < 0.05$ ), but not in the control group ( $34.4 \pm 9.4$  to  $38.3 \pm 8.8$   $\mu\text{mol/ml}$ ).

## **CONCLUSION:**

Waon therapy mobilized circulating endothelial progenitor cells and improved limb ischemia in patients with PAD. Waon therapy is a highly promising therapy for patients with PAD.

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PMID: 20843662 [PubMed - indexed for MEDLINE]

## **Paper 7**

Am J Cardiol. 2012 Jan 1;109(1):100-4. Epub 2011 Sep 23.

### **Effect of repeated sauna treatment on exercise tolerance and endothelial function in patients with chronic heart failure.**

Ohori T, Nozawa T, Ihori H, Shida T, Sobajima M, Matsuki A, Yasumura S, Inoue H.

#### **Source**

Second Department of Internal Medicine, Graduate School of Medicine, University of Toyama, Japan.

#### **Abstract**

Repeated sauna treatment, known as Waon therapy, has been shown to improve cardiac function as well as exercise tolerance in patients with chronic heart failure. However, the underlying mechanisms of this therapy regarding these improvements remain to be elucidated. Forty-one patients with chronic heart failure (mean age  $68.3 \pm 13.5$  years old) underwent Waon therapy 5 times a week for 3 weeks. Before and after treatment, a number of assessments were performed in all subjects: 6-minute walk test, echocardiography, determination of neurohumoral factors and number of circulating CD34(+) cells, and a flow-mediated dilation (FMD) test of endothelial function. Cardiopulmonary exercise testing was also performed in 20 patients. Waon therapy increased the left ventricular ejection fraction (from  $30.4 \pm 12.6\%$  to  $32.5\% \pm 12.8\%$ ,  $p = 0.023$ ) and reduced plasma levels of norepinephrine (from  $400 \pm 258$  to  $300 \pm 187$   $\text{pg/ml}$ ,  $p = 0.015$ ) and brain natriuretic peptide (from  $550 \pm 510$  to  $416 \pm 431$   $\text{pg/ml}$ ,  $p = 0.035$ ). Waon therapy increased the 6-minute walk distance (from  $337 \pm 120$  to  $379 \pm 126$  m,  $p < 0.001$ ) in association with an improvement in FMD (from  $3.5 \pm 2.3\%$  to  $5.5\% \pm 2.7\%$ ,  $p < 0.001$ ) and an increase in the number of circulating CD34(+) cells ( $p = 0.025$ ). Changes in 6-minute walk distance were correlated positively with those in the left ventricular ejection fraction and FMD and negatively with those in plasma levels of norepinephrine and brain natriuretic peptide levels. A multivariate analysis revealed that an increase in FMD was the only independent determinant of 6-minute walk distance improvement. Finally, Waon therapy significantly increased peak  $\text{Vo}(2)$ , and this increase was also correlated with changes in FMD. In conclusion, repeated sauna therapy in patients with chronic heart failure improves exercise tolerance in association with improvement in endothelial function.

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PMID: 21944673 [PubMed - indexed for MEDLINE]



# Annex B

## SKIN AND ANNEXES

### Paper 1

J Dermatolog Treat. 2011 Dec;22(6):366-71. Epub 2011 Jan 22.

### **Balneotherapy for atopic dermatitis in children at Comano spa in Trentino, Italy.**

Farina S, Gisondi P, Zanoni M, Pace M, Rizzoli L, Baldo E, Girolomoni G.

#### **Source**

Department of Medicine, Section of Dermatology and Venereology, University of Verona, Verona, Italy.

#### **Abstract**

#### **BACKGROUND:**

No controlled studies have investigated whether balneotherapy is effective in atopic dermatitis (AD).

#### **OBJECTIVES:**

To investigate the efficacy and safety of balneotherapy performed at Comano spa (Trentino, Italy) compared to topical corticosteroids (TCS) in the treatment of AD.

#### **METHODS:**

This was an open, randomized, clinical trial including 104 children (aged 1-14 years) with mild to moderate AD who were assigned either to balneotherapy (n = 54) or TCS (n = 50) once daily for 2 weeks. AD severity and quality of life were measured using the SCORAD, investigator global assessment (IGA), patients' self global assessment (PSGA), children's dermatology life quality index (CDLQI) and family dermatitis impact questionnaire (FDIQ). Subjective measures were re-evaluated 4 months after the end of therapy.

#### **RESULTS:**

Balneotherapy and TCS resulted in a significant reduction of all parameters at week 2. TCS were more effective than balneotherapy regarding SCORAD ( $46\% \pm 7.71$  vs  $26\% \pm 9.4$ , mean  $\pm$  SD;  $p < 0.03$ ). In contrast, IGA, PSGA, CDLQI and FDIQ improvement was similar. At month 4, the number and duration of relapses were less in patients treated with balneotherapy compared to those treated with TCS ( $p < 0.0001$ ).

#### **CONCLUSIONS:**

Balneotherapy at Comano spa appears to be beneficial in children with mild to moderate AD.

PMID: 21254853 [PubMed - indexed for MEDLINE]

### Paper 2

Int J Dermatol. 2000 Jan;39(1):59-69.

## **Climatotherapy of atopic dermatitis at the Dead Sea: demographic evaluation and cost-effectiveness.**

Harari M, Shani J, Seidl V, Hristakieva E.

### **Source**

DMZ-MOR Rehabilitation Clinic, Ein-Bokek (The Dead Sea), Israel.

### **Abstract**

**BACKGROUND:** About 21% of the patients coming yearly to the DMZ Clinic at the Dead Sea for climatotherapy suffer from atopic dermatitis. This is a common, chronic, and relapsing disease which necessitates drug treatment (topical corticosteroids, antimicrobials, antihistamines, or immunomodulators), phototherapy, or climatotherapy. **Objective and methods** As the improvement in the condition of patients after 4 weeks of climatotherapy at the Dead Sea is remarkable, we undertook to evaluate the demographic factors that have the strongest impact on this beneficial effect, in adults and children. The major factors studied were: gender, previous medical history, previous stays at the Dead Sea, skin type, skin involvement, age, and duration of treatment. **Results** A retrospective study of 1718 patients revealed that previous treatments at the Dead Sea and stays longer than 4 weeks caused a clearance greater than 95%, the length of sun exposure was no longer than 5 h daily, and there was no impact of the percentage of skin involvement on the clearance of patients staying more than 4 weeks. **CONCLUSION:** Climatotherapy of atopic dermatitis at the Dead Sea is a highly effective modality for treating this disease. It is also a highly cost-effective method, as the patients take no medications and experience no side-effects. Successful climatotherapy of atopic dermatitis requires strict medical supervision throughout the whole length of the patient's stay on shore.

PMID: 10651969 [PubMed - indexed for MEDLINE]

### **Paper 3**

Dermatitis. 2012 Mar;23(2):75-80.

## **Climatotherapy at the dead sea: an effective treatment modality for atopic dermatitis with significant positive impact on quality of life.**

Adler-Cohen C, Czarnowicki T, Dreiherr J, Ruzicka T, Ingber A, Harari M.

### **Source**

From the \*RIDS: The Joint Research Institute on Climatotherapy for Skin Diseases at the Dead Sea, The Deutsches Medizinisches Zentrum Medical Center and the Department of Dermatology, Hadassah University Medical Center, Jerusalem, Israel, in cooperation with The Department of Dermatology, Ludwig Maximilian University Hospital, Munich, Germany; and †Siaal Research Center, Division of Health in the Community, Ben-Gurion University of the Negev, Beer Sheva, Israel.

### **Abstract**

#### **BACKGROUND:**

Atopic dermatitis (AD) has an appreciable effect on quality of life. Improving the quality of life of AD patients is a priority.

## **OBJECTIVE:**

This study aimed to evaluate the impact of Dead Sea climatotherapy (DSC) as a treatment of AD and its influence on the quality of life of these patients.

## **METHODS:**

Forty-nine adult patients with AD treated during the years 2009-2010 at the Deutsches Medizinisches Zentrum Medical Center participated in this prospective study. Climatotherapy was administered in accordance with a computer-designed protocol and included gradually increased sun exposure after a sea bath. Severity of AD was evaluated using the Scoring Atopic Dermatitis (SCORAD) index. Patient quality of life was evaluated using Skindex-29. Statistical analysis was performed using a paired t test and Wilcoxon and Mann-Whitney U tests.

## **RESULTS:**

After treatment, the mean SCORAD value improved by 39 points ( $P < 0.001$ ). The overall Skindex-29 score improved by a mean value of 33 points ( $P < 0.001$ ). The pretreatment SCORAD, duration of AD, and maximal daily sun exposure predicted the posttreatment SCORAD values. Pretreatment Skindex-29 and patient age predicted the posttreatment Skindex-29 in a multiple linear regression model.

## **CONCLUSIONS:**

Dead Sea climatotherapy provides an effective treatment modality for AD by improving the patient's skin condition and quality of life.

PMID: 22653123 [PubMed - in process]

## **Paper 4**

Eur J Dermatol. 2002 Nov-Dec;12(6):543-8.

### **Dead Sea treatment - principle for outpatient use in atopic dermatitis: safety and efficacy of synchronous balneophototherapy using narrowband UVB and bathing in Dead Sea salt solution.**

Schiffner R, Schiffner-Rohe J, Gerstenhauer M, Landthaler M, Hofstädter F, Stolz W.

#### **Source**

Department of Dermatology, University of Regensburg, Germany. jr.schiffner@t-online.de

#### **Abstract**

Safety and efficacy of this new treatment modality for out-patients were evaluated by an uncontrolled multicenter trial under GCP-conditions. Patients had to undergo 3-5 treatment sessions per week up to 35 in total. SCORAD (SC) was assessed at baseline, after 20 and 35 sessions. For patients with early study withdrawal the last-observation-carry-forward-principle was used. 615 intention-to-treat (itt)- (baseline SC: 59.4) and 143 according-to-protocol (atp)-patients (baseline SC: 60.1) could be analysed. 289 patients (47%) (baseline SC: 59.1) underwent less than 35 sessions. Main reasons were: lack of time (16%), non-compliance (12%), good improvement (7%), lack of efficacy (6%), intercurrent disease (4%) and side effects (3%). Mean number of sessions in atp-group was 35, in itt 26, and in patients with early study withdrawal 15.8. SC

decreased in atp-group to 37.5 (itt: 44.5/patients with early study withdrawal: 46.1) after 20 sessions and to 27.1 (35.2/42.6) at end of treatment. Relative SC-improvement was statistically significant in atp- (55%), itt-group (41%), and in patients with early study withdrawal (26%). Most frequent side effects were: erythema in 7.3%, burning of skin due to salt solution in 3.6%. Safety and efficacy could be proven in both atp- and itt-group. A marked difference in efficacy between atp and itt underlines the importance of evaluating itt-data providing a more realistic assessment of a treatment modality in practice. This treatment is especially recommended for patients with chronic type of AD, high compliance and time free for therapy.

## Comment in

The 'Dead-Sea thyrotoxicosis': a side-effect of the Dead-Sea climatotherapy? [Eur J Dermatol. 2003]

PMID: 12459524 [PubMed - indexed for MEDLINE] [Free full text](#)

## Paper 5

J Eur Acad Dermatol Venereol. 2011 Jul;25(7):765-73. doi: 10.1111/j.1468-3083.2010.03857.x. Epub 2010 Oct 3.

### **A first prospective randomized controlled trial on the efficacy and safety of synchronous balneophototherapy vs. narrow-band UVB monotherapy for atopic dermatitis.**

Heinlin J, Schiffner-Rohe J, Schiffner R, Einsele-Krämer B, Landthaler M, Klein A, Zeman F, Stolz W, Karrer S.

## Source

Department of Dermatology, University of Regensburg, Center for Clinical Studies, University Hospital Regensburg, Regensburg, Germany.

## Abstract

### **BACKGROUND:**

Data from an uncontrolled trial suggest synchronous balneophototherapy (sBPT), which simulates treatment conditions at the Dead Sea, to be effective in the management of atopic dermatitis (AD).

### **OBJECTIVES:**

The purpose of this prospective randomized controlled study was to compare the efficacy and safety of sBPT with narrow-band (NB) UVB monotherapy (PT) for AD.

### **METHODS:**

In this phase III multicentre trial, 180 patients with moderate-to-severe AD were allocated to two groups in a 1:1 ratio; group 1 received sBPT consisting of NB UVB treatment and synchronous bathing in 10% Dead Sea salt solution, group 2 monotherapy with UVB 311 nm. The confirmatory study design consisted of up to 35 treatment sessions. Primary endpoint, analysed on an intention-to-treat-basis (n=169), was the relative improvement of the severity SCORing of the Atopic Dermatitis Index (SCORAD) from baseline to the end of treatment (35 sessions or early cure). Sample-size calculation aimed at establishing at least 15% superiority.

## RESULTS:

SCORing of the Atopic Dermatitis Index at baseline was comparable between sBPT (61.8±14.1) and PT (61.5±12.4) group. At the end of therapy, a clinically relevant and statistically significant difference of 26.2% could be shown (P<0.001). Exploratory testing showed statistically significant superiority of sBPT after 6 months. Mild adverse events more frequently occurred in the sBPT group (n=46, PT: n=31), whereas more patients withdrew early because of adverse events in the PT group (n=6, sBPT: n=2).

## CONCLUSIONS:

A clear advantage of sBPT in comparison to PT was proven. Tolerability was comparable; both treatments showed to be safe.

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PMID: 21029208 [PubMed - indexed for MEDLINE]

## Paper 6

Hautarzt. 1999 Sep;50(9):649-53.

### **Comparison of balneophototherapy and UVA/B mono-phototherapy in patients with subacute atopic dermatitis.**

[Article in German]

Dittmar HC, Pflieger D, Schempp CM, Schöpf E, Simon JC.

#### **Source**

Universitäts-Hautklinik Freiburg, Freiburg.

#### **Abstract**

In a controlled prospective study we compared the efficacy of combined salt water bath and UVA/B phototherapy to a UVA/B mono-phototherapy in patients with subacute atopic dermatitis (AD). The patients in the balneophototherapy group (n=16) were treated with baths containing 3-5% of the synthetic salt Psoriasisal(trade mark), followed immediately by UVA/B irradiation, while the other treatment arm (n=12) received UVA/B phototherapy alone. After 20 treatments the balneophototherapy group showed a statistically significant (p<=0.0015) reduction of the SCORAD score from 69.5 before to 36.8 after therapy. No statistically significant reduction in the SCORAD score could be observed in the UVA/B phototherapy group (50.6 before to 44.3 after therapy). The cumulative UVB dose was significantly lower in the balneophototherapy group (0.9 J/cm<sup>2</sup>) as compared to the UVA/B monotherapy group (2.0 J/cm<sup>2</sup>). Balneophototherapy was well tolerated by patients with atopic dermatitis and no side effects were observed. We conclude that balneophototherapy expands the therapeutic options for patients with subacute atopic dermatitis.

PMID: 10501681 [PubMed - indexed for MEDLINE]

## Paper 7

Int J Dermatol 2005;44:151-7.

### **Bathing in a magnesium rich Dead Sea salt solution improves skin barrier function, enhances skin**

## **hydration and reduces inflammation in atopic dry skin.**

Proksch E, Nissen HP, Bremgartner M, Urquhart C.

### **Abstract**

Magnesium salts, the prevalent minerals in Dead Sea water, are known to exhibit favorable effects in inflammatory diseases. We examined the efficacy of bathing atopic subjects in a salt rich in magnesium chloride from deep layers of the Dead Sea (Mavena(R) Dermaline Mg(46) Dead Sea salt, Mavena AG, Belp, Switzerland). Volunteers with atopic dry skin submerged one forearm for 15 min in a bath solution containing 5% Dead Sea salt. The second arm was submerged in tap water as control. Before the study and at weeks 1-6, transepidermal water loss (TEWL), skin hydration, skin roughness, and skin redness were determined. We found one subgroup with a normal and one subgroup with an elevated TEWL before the study. Bathing in the Dead Sea salt solution significantly improved skin barrier function compared with the tap water-treated control forearm in the subgroup with elevated basal TEWL. Skin hydration was enhanced on the forearm treated with the Dead Sea salt in each group, which means the treatment moisturized the skin. Skin roughness and redness of the skin as a marker for inflammation were significantly reduced after bathing in the salt solution. This demonstrates that bathing in the salt solution was well tolerated, improved skin barrier function, enhanced stratum corneum hydration, and reduced skin roughness and inflammation. We suggest that the favorable effects of bathing in the Dead Sea salt solution are most likely related to the high magnesium content. Magnesium salts are known to bind water, influence epidermal proliferation and differentiation, and enhance permeability barrier repair.

[\[PUBMED\]](#) [\[FULLTEXT\]](#)

### **Paper 8**

Hautarzt. 2010 Aug;61(8):683-90.

## **Psoriasis. Natural vs artificial balneophototherapy.**

[Article in German]

Roos S, Hammes S, Ockenfels HM.

### **Source**

Haut- und Allergieklinik Hanau, Klinikum Hanau GmbH, Leimenstr. 20, 63450, Hanau, Deutschland.

### **Abstract**

Artificial balneophototherapy is an imitation of the natural balneophototherapy (Dead Sea climatotherapy; DSC) using highly concentrated salt solutions (25%) and UVB radiation. In 2008 the artificial balneophototherapy was included in the German healthcare system as an effective, evidence-based therapy for patients with moderate-severe psoriasis. In contrast, natural DSC is still considered a "non-standard and off-label therapy". Therefore we analyzed all studies published in the past two decades on both artificial and natural balneophototherapy comparing them in effectiveness, length of remission and practicability. Evidence-based studies on DSC showed good clinical results and long remission periods in psoriatic patients; the two methods seem comparable in effectiveness. Patients with chronic, therapy-resistant psoriasis should have access to DSC if they fail routine measures.

## Comment in

[On the article: "Psoriasis. Natural versus artificial balneophototherapy]. [Hautarzt. 2011]  
PMID: 20607200 [PubMed - indexed for MEDLINE]

### Paper 9

Photodermatol Photoimmunol Photomed. 2001 Feb;17(1):22-5.

#### **Balneophototherapy of psoriasis: highly concentrated salt water versus tap water--a randomized, one-blind, right/left comparative study.**

Gambichler T, Rapp S, Senger E, Altmeyer P, Hoffmann K.

#### **Source**

Department of Dermatology, Ruhr-University Bochum, Rödermark, Germany.  
t.gambichler@derma.de

#### **Abstract**

##### **BACKGROUND/PURPOSE:**

Apart from climatotherapy and spa therapy, combined treatment with salt water baths and artificial UV radiation (balneophototherapy) has been advocated for the treatment of psoriasis. As there is a lack of controlled studies on balneophototherapy (BPT), we conducted a randomized, one-blind, right/left comparison with salt water versus tap water in order to investigate the significance of the salt concentration in the efficacy of BPT.

##### **METHODS:**

Ten psoriasis patients with chronic plaques on the elbows were included in the study. One elbow was soaked in 24% NaCl solution and the other in tap water. Subsequently, broadband UVB irradiation was administered. BPT was performed 4 times weekly with a total of 30 treatments.

##### **RESULTS:**

A highly significant ( $P < 0.001$ ) decrease of the clinical baseline score was observed after 30 treatments; however, there was no significant ( $P > 0.5$ ) difference in clearance of the psoriatic lesions between the sites soaked in salt water and tap water.

##### **CONCLUSION:**

Our results suggest that any additional benefit of soaking in salt water and tap water in BPT are unlikely to be due to the salinity of the liquids.

PMID: 11169172 [PubMed - indexed for MEDLINE]

### Paper 10

J Altern Complement Med. 2007 Sep;13(7):725-32.

#### **A pragmatic randomized controlled trial on the effectiveness of highly concentrated saline spa water**

## **baths followed by UVB compared to UVB only in moderate to severe psoriasis.**

Brockow T, Schiener R, Franke A, Resch KL, Peter RU.

### **Source**

Spa Medicine Research Institute, Bad Elster, Germany. thomas.brockow@d-i-g.org

### **Abstract**

#### **BACKGROUND:**

There is a lack of sufficiently large randomized trials evaluating the effectiveness of saline spa balneophototherapy compared to ultraviolet B (UVB) only.

#### **OBJECTIVE:**

The study aimed to evaluate whether highly concentrated saline spa water baths followed by UVB (HC-SSW-UVB) are superior to UVB only in moderate to severe psoriasis.

#### **METHODS:**

One hundred and sixty (160) adults with a Psoriasis Area and Severity Index (PASI) of >10 from 4 German spa centers were randomly allocated to HC-SSW-UVB (local sodium chloride concentration between 25% and 27%) or UVB only 3 a week until remission (PASI < 5) or for a maximum of 6 weeks. Reduction of PASI > or = 50% (PASI-50) at the end of the intervention period was defined as primary outcome. Only persons receiving at least 1 intervention were included into the primary analysis.

#### **RESULTS:**

Participants allocated to HC-SSW-UVB attained to a statistically significantly higher rate of PASI-50 than patients allocated to UVB only (68/79 [86%] versus 38/71 [54%];  $p < 0.001$ ; number needed to treat, 3.1; 95% confidence interval, 2.1-6.0). Postintervention analysis did not yield a clear hint of a persisting effect.

#### **CONCLUSIONS:**

The study indicates that HC-SSW-UVB are superior to routine UVB at the end of a 6-week treatment course.

PMID: 17931065 [PubMed - indexed for MEDLINE]

## **Paper 11**

J Eur Acad Dermatol Venereol. 2005 Sep;19(5):578-81.

## **Synchronous balneophototherapy is effective for the different clinical types of psoriasis.**

Holló P, Gonzalez R, Kása M, Horváth A.

### **Source**

Department of Dermatovenereology and Dermatoooncology Semmelweis Medical School, Budapest, Hungary. holpet@bor.sote.hu

### **Abstract**



## **BACKGROUND:**

The efficacy of synchronous balneophototherapy in clearing psoriasis is based on the multiple-targeted effects of UVB light and Dead Sea salt. Their synchronous application produces a synergic effect.

## **OBJECTIVE:**

The purpose of this retrospective study is: 1) to evaluate the efficacy of synchronous balneophototherapy for treating different clinical types of psoriasis; 2) to determine whether there is any difference between response to treatment, and 3) to gain more data in order to predict the effect of treatment in different clinical types, and thus to support the selection of patients for treatment.

## **METHODS:**

Patients received a basic course of synchronous balneophototherapy according to the Regensburg scheme, consisting of 35 treatment sessions, followed by a maintenance course of a further 25 treatments. The patients' skin status was monitored by weekly assessment using the PASI score throughout the course. The efficacy of the treatment was evaluated through the results of 373 patients treated according to protocol during the basic course, and the results of 78 of these patients during the maintenance course. One hundred and eighty-six patients were enrolled into the study comparing the efficacy of the basic course for the different clinical types of psoriasis: data of patients with large plaques, small plaques, guttate and confluating type of skin signs were summarized and compared.

## **RESULTS:**

During the basic course of treatment 70.7% improvement of the average PASI index was observed; the average PASI index decreased from 16.14 to 4.73. A further improvement from 4.58 to 4.27 of the average PASI was found during the maintenance therapy. Small plaque-type skin signs showed the best response with a PASI decrease of 76.1%; Guttate type had a PASI decrease of 73.7%, large plaque type, 67.1% and confluating type, 62%. Comparing data with the average PASI decrease, a statistically significant lower decrease was found in confluating type cases.

## **CONCLUSIONS:**

These results confirm that synchronous balneophototherapy is an effective treatment modality for different clinical types of psoriasis. Patients with small plaques have the greatest chance of the most marked clinical clearing; guttate and large plaque types of psoriasis also respond well to the treatment.

PMID: 16164712 [PubMed - indexed for MEDLINE]

## **Paper 12**

Yonsei Med J. 2009 Apr 30;50(2):215-21.

## **Quality of life of psoriasis patients before and after balneo -- or balneophototherapy.**

Tabolli S, Calza A, Di Pietro C, Sampogna F, Abeni D.

### **Source**

Health Services Research Unit, Istituto Dermopatico dell'Immacolata (IDI-IRCCS), Rome, Italy. ste.tab@idi.it

### **Abstract**

## **PURPOSE:**

An observational prospective study was conducted to study the effects of hypotonic spa-water baths and narrowband ultraviolet B therapy given alone or in combination for treatment of moderate-severe psoriasis.

## **MATERIALS AND METHODS:**

TWO TREATMENTS WERE ANALYSED: 2 weeks of balneotherapy followed by ultraviolet-B (UVB) 311-nm phototherapy (BPT) or 2 weeks of daily bath treatments of Comano water alone (BT). One hundred and eleven adult patients with moderate to severe chronic plaque psoriasis were enrolled. Quality of life (QoL) questionnaires {36-item Short Form of the Medical Outcomes Study questionnaire (SF-36) and Skindex-29} were administered at baseline and 2 months from the end of therapy. The self-administered Psoriasis Area Severity Index (SAPASI), and the General Health Questionnaire (GHQ)-12 (to assess clinical severity and psychological distress, respectively) were also recorded at the same time-periods.

## **RESULTS:**

SAPASI was significantly reduced from 15.2 to 8.7 in BPT group and 11.6 to 7.8 in BT. A decrease of greater than 50% after therapy in SAPASI\_50 score was reached by 42% and 37% of patients in the BPT and BT groups, respectively. At follow-up, both groups had better scores on all SF-36 scales (with statistically significant improvement in social functioning and mental health in the BPT group) and in all Skindex-29 scales. A statistically significant reduction of GHQ-12 positive cases was observed in the BPT group.

## **CONCLUSION:**

Comano spa-water alone or in combination with phototherapy had beneficial therapeutic effects on patients with psoriasis. Although our observational study design prevents us from making meaningful comparisons between the 2 interventions, the combination of balneo and phototherapy seems to improve QoL and lessen clinical severity, and reduced the proportion of GHQ-12 positive cases.

PMID: 19430554 [PubMed - indexed for MEDLINE] PMCID: PMC2678696

**Free PMC Article**

## **Paper 13**

J Eur Acad Dermatol Venereol. 2011 May;25(5):570-8. doi: 10.1111/j.1468-3083.2010.03840.x. Epub 2010 Sep 14.

**A randomized clinical trial in psoriasis: synchronous balneophototherapy with bathing in Dead Sea salt solution plus narrowband UVB vs. narrowband UVB alone (TOMESA-study group).**

Klein A, Schiffner R, Schiffner-Rohe J, Einsele-Krämer B, Heinlin J, Stolz W, Landthaler M.

## **Source**

Department of Dermatology, University Hospital Regensburg, Regensburg, Germany. annette.klein@klinik.uni-regensburg.de

## **Abstract**

## **BACKGROUND:**

Synchronous balneophototherapy (sBPT) simulates treatment conditions at the Dead Sea for outpatient use. In the past, sBPT proved to be an effective treatment for psoriasis. However, there is a lack of sufficiently large randomized controlled clinical trials evaluating the additional benefit of sBPT compared with ultraviolet B (UVB) monotherapy.

## **OBJECTIVES:**

The purpose of this study was to compare the effectiveness and safety of sBPT with UVB phototherapy (PT) alone in a randomized controlled effectiveness study.

## **METHODS:**

In this phase III, multicentre effectiveness study, 367 patients with moderate to severe psoriasis were randomly allocated in a 1 : 1 ratio to receive either sBPT consisting of narrowband UVB PT with 311 nm and synchronous bathing in 10% Dead Sea salt solution or PT with 311 nm alone. Primary endpoint, analysed on an intention-to-treat basis (n = 356), was the relative improvement of the Psoriasis Area and Severity Index (PASI) from baseline to end of treatment (35 sessions or clearance). Sample size calculation aimed at the detection of superiority of at least 10%.

## **RESULTS:**

Median PASI values were comparable at baseline (sBPT: 15.1, interquartile range: 10.9-24.3; PT: 15.3, interquartile range: 10.0-23.7). A clinically relevant and statistically significant difference of 49.5% between sBPT and PT could be proven at the end of the therapy phase (P < 0.001; Wilcoxon-Mann-Whitney test). Exploratory testing showed a statistically significant superiority of sBPT after 6 months.

## **CONCLUSIONS:**

In routine clinical practice, sBPT is superior to PT alone after 35 treatment sessions and a follow-up of 6 months. Both treatments demonstrated to be safe. © 2010 The Authors. Journal of the European Academy of Dermatology and Venereology © 2010 European Academy of Dermatology and Venereology.

PMID: 20840347 [PubMed - indexed for MEDLINE]

## **Paper 14**

Br J Dermatol. 2000 Apr;142(4):740-7.

## **Evaluation of a multicentre study of synchronous application of narrowband ultraviolet B phototherapy (TL-01) and bathing in Dead Sea salt solution for psoriasis vulgaris.**

Schiffner R, Schiffner-Rohe J, Wöfl G, Landthaler M, Glässl A, Walther T, Hofstädter F, Stolz W.

## **Source**

Department of Dermatology, University of Regensburg, Germany.

## **Abstract**

The synchronous application of narrowband UVB phototherapy with 311 nm lamps (Philips TL-01) and bathing in Dead Sea salt solution was evaluated in a multicentre trial (n = 60) in outpatients suffering from psoriasis vulgaris. The study design consisted of an initial therapy phase of up to 35 treatments (three to five times a week) followed by maintenance therapy with up to 35 further applications (once or twice a week). Evaluation was performed separately for patients in according-to-protocol (ATP) (n = 280) and intention-to-treat (ITT) (n = 692) groups. An overall significant improvement of the Psoriasis Area and Severity Index (PASI) score ( $P < 0.05$ ) could be shown for both groups during initial therapy with 71.4% improvement for ATP and 61% for ITT patients. The mean PASI for ATP (values for ITT in parentheses) was 17.7 (18.6) at baseline, 9.5 (10.7) after 20 applications and 5.2 (7.4) at the end of initial therapy. On average, ATP patients received 3.9 (3.5) applications per week with a cumulative irradiation dose of 19.5 J cm<sup>-2</sup> (16.2 J cm<sup>-2</sup>). The most frequent side-effect was erythema, observed in 8.7% of the patients. Subjective evaluation of the therapy by the patients (n = 168) was excellent. Seventy-nine per cent of patients preferred the new treatment strategy in comparison with other previous therapies and 88% regarded this therapy as pleasant and comfortable. In conclusion, we could demonstrate a significant effect of therapy in both the ATP and the ITT groups for this new treatment system which imitates, as far as possible, the Dead Sea climatic conditions, with no severe side-effects and a high acceptance by the patients.

PMID: 10792225 [PubMed - indexed for MEDLINE]

## Paper 15

Br J Dermatol. 2005 Sep;153(3):613-9.

### **A randomized controlled comparison of the efficacy of Dead Sea salt balneophototherapy vs. narrowband ultraviolet B monotherapy for chronic plaque psoriasis.**

Dawe RS, Yule S, Cameron H, Moseley H, Ibbotson SH, Ferguson J.

#### **Source**

Photobiology Unit, Department of Dermatology, University of Dundee, Ninewells Hospital and Medical School, Dundee DD1 9SY, UK. r.s.dawe@dundee.ac.uk

#### **Abstract**

##### **BACKGROUND:**

Dead Sea (DS) salt solution soaks are used in combination with narrowband ultraviolet B (NB-UVB) to treat psoriasis in many centres, particularly in continental Europe. No previously published controlled study has assessed DS salt + NB-UVB balneophototherapy.

##### **OBJECTIVES:**

To compare DS salt balneophototherapy with NB-UVB monotherapy for chronic plaque psoriasis.

##### **METHODS:**

Sixty patients with chronic plaque psoriasis participated in this paired, controlled study, with pretreatment DS salt soaks randomly allocated to each participant's right or left study limb. Psoriasis severity was assessed with a Scaling, Erythema and Induration score by a blinded observer. Assessments were weekly during

the therapy course, and thereafter 8-weekly until relapse or for up to 1 year after clearance.

### **RESULTS:**

The mean area under the psoriasis severity-time curves during treatment was not detectably lower with DS salt balneophototherapy than with NB-UVB monotherapy (P = 0.099). The psoriasis severity score fell slightly more from beginning to end of courses with DS salt balneophototherapy than with NB-UVB monotherapy (P = 0.019). There was no detectable difference in times to relapse.

### **CONCLUSIONS:**

In this population the addition of pretreatment DS salt soaks to NB-UVB did not result in a clinically important improvement in clearance of psoriasis.

### **Comment in**

Controlled clinical trials on balneophototherapy in psoriasis.  
[Br J Dermatol. 2006]

PMID: 16120152 [PubMed - indexed for MEDLINE]

### **Paper 16**

J Eur Acad Dermatol Venereol. 2007 Sep;21(8):1027-37.

### **A pragmatic randomized controlled trial on the effectiveness of low concentrated saline spa water baths followed by ultraviolet B (UVB) compared to UVB only in moderate to severe psoriasis.**

Brockow T, Schiener R, Franke A, Resch KL, Peter RU.

### **Source**

Spa Medicine Research Institute, Bad Elster, Germany. thomas.brockow@d-i-g.org

### **Abstract**

#### **OBJECTIVE:**

To evaluate whether low concentrated saline spa water baths followed by ultraviolet B (LC-SSW-UVB) are superior to UVB alone in moderate to severe psoriasis.

#### **BACKGROUND:**

There is a lack of sufficiently large randomized controlled clinical trial evaluating the additional benefit of saltwater baths followed by UVB compared to UVB only in psoriasis.

#### **STUDY DESIGN:**

Partly evaluator blind, multicentre, pragmatic, randomized controlled trial.

#### **SETTING:**

Five German spa centres.

## **SUBJECTS:**

One hundred and forty-three adults with stable psoriasis during the last month and a Psoriasis Area and Severity Index (PASI) of > 10 and/or an affected body surface area of > 15%.

## **INTERVENTIONS:**

LC-SSW-UVB or UVB thrice a week until remission (PASI < 5) or for a maximum of 6 weeks. Sodium chloride concentrations of natural springs varied between 4.5% and 12%. Conventional UVB (broadband UVB or selective UVB phototherapy) was used as irradiation source.

## **MAIN OUTCOME:**

Reduction of PASI and/or affected body surface area of 50% at the end of the intervention period (PASI-50). Only participants receiving at least one intervention were included in the primary analysis.

## **RESULTS:**

Patients allocated to LC-SSP-UVB attained a statistically significantly higher rate of PASI-50 at the end of the intervention period than patients allocated to UVB [58/79 (73%) vs. 32/64 (50%); P = 0.01; NNT, 4.3, 95% CI, 2.4-18.1]. Benefit persisted until 3 months only for one of two secondary outcomes considered.

## **CONCLUSIONS:**

In routine clinical practice balneophototherapy using conventional UVB is superior to conventional UVB only at the end of a 6-week treatment course.  
PMID: 17714121 [PubMed - indexed for MEDLINE]

## **Paper 18**

Arch Dermatol. 2001 Aug;137(8):1035-9.

### **Saline spa water or combined water and UV-B for psoriasis vs conventional UV-B: lessons from the Salies de Béarn randomized study.**

Léauté-Labrèze C, Saillour F, Chêne G, Cazenave C, Luxey-Bellocq ML, Sanciaume C, Toussaint JF, Taïeb A.

#### **Source**

Service de Dermatologie, Hôpital Saint André, 1 rue Jean Burguet, 33075 Bordeaux CEDEX, France.

#### **Abstract**

#### **OBJECTIVE:**

To study the effects of UV-B therapy and saline spa water given alone or in combination for the treatment of psoriasis.

#### **DESIGN:**

Randomized, controlled, comparative study with blinded observers.

#### **SETTING:**

Salies de Béarn, saline spa water center located in the southwest of France.

## **PARTICIPANTS:**

Seventy-one adult patients with psoriasis with a Psoriasis Area and Severity Index (PASI) score greater than 10.

## **INTERVENTION:**

Patients were randomly assigned to 1 of 3 treatments: spa water alone (group A); UV-B 311-nm phototherapy alone (group B); and a combination of the 2 therapies (group C). The 3 groups were treated on a daily basis 5 days a week for a total of 21 days.

## **MAIN OUTCOME MEASURES:**

Change in PASI score from baseline as determined by an investigator blinded to randomization; variation in quality of life, adverse effects, and long-term effects (1 year after treatment).

## **RESULTS:**

Four patients dropped out because of secondary effects. Efficacy was similar in groups B and C, with changes in PASI of -64% and -55%, respectively at 3 weeks. For group A, change in PASI was -29%, thus showing a minor therapeutic effect of saline spa water alone and poor efficacy compared with groups B and C ( $P < .001$ ). More adverse effects were reported in groups A and C but did not reach significance. Combined saline spa water and UV-B therapy had no sparing effect on UV-B dosages. One year after treatment, no long-term benefit could be attributed specifically to a given regimen, but the patients had overall significantly better PASI scores than at baseline.

## **CONCLUSIONS:**

Saline spa water alone had a minor therapeutic effect in psoriasis, and the beneficial effect of bathing to enhance phototherapy was not demonstrated.

## **Comment in**

[Saline Spa water and UV-B for psoriasis.](#) [Arch Dermatol. 2002]

PMID: 11493096 [PubMed - indexed for MEDLINE]

## **Paper 19**

Arch Dermatol. 2007 May;143(5):586-96.

## **Bath PUVA and saltwater baths followed by UV-B phototherapy as treatments for psoriasis: a randomized controlled trial.**

Schiener R, Brockow T, Franke A, Salzer B, Peter RU, Resch KL.

## **Source**

Department of Dermatology, University of Ulm, Germany.

## **Abstract**

## **OBJECTIVE:**

To evaluate the efficacy of psoralens dissolved in a warm-water bath followed by exposure to UV-A irradiation (bath PUVA) or saltwater phototherapy (SW UV-B) compared with tap-water phototherapy (TW UV-B) or UV-B irradiation alone in psoriasis.

**DESIGN:**

Multisite, prospective, randomized, controlled trial with 4 parallel groups.

**SETTING:**

Total of 102 dermatologic outpatient clinics.

**PATIENTS:**

Total of 1241 patients with stable psoriasis vulgaris and a Psoriasis Area and Severity Index score of 7 or greater.

**INTERVENTIONS:**

Four-times-weekly UV-B, TW UV-B, SW UV-B, or bath-PUVA with baths preceding UV irradiation over a maximum of 8 weeks. The UV dose was adapted to erythema response.

**MAIN OUTCOME MEASURES:**

Incidence of therapeutic success, defined as a reduction of the Psoriasis Area and Severity Index or affected body surface area of 50% or more.

**RESULTS:**

Patients who received TW UV-B had a significantly higher incidence of therapeutic success than did patients treated with UV-B alone (60.7% vs 43.3%;  $P < .001$ ; number needed to treat, 5.8; 95% confidence interval [CI], 3.9-10.9). Patients who received SW UV-B or bath PUVA had a significantly higher incidence of therapeutic success than did patients treated with TW UV-B (74.9% vs 60.7%;  $P < .001$ ; number needed to treat, 7.0; 95% CI, 4.6-14.9; and 78.4% vs 60.7%;  $P < .001$ ; number needed to treat, 5.7; 95% CI, 4.0-9.7, respectively). Bath PUVA was not superior to SW UV-B (78.4% vs 74.9%;  $P = .34$ ).

**CONCLUSION:**

Bath PUVA and SW UV-B are comparably effective treatments in psoriasis and superior to UV-B and TW UV-B.

**Comment in**

Balneophototherapy for psoriasis using saltwater baths and UV-B irradiation, revisited. [Arch Dermatol. 2007]

PMID: 17519218 [PubMed - indexed for MEDLINE]

**Paper 20**

Rheumatol Int. 2000;19(3):77-82.

**Immediate and delayed effects of treatment at the Dead Sea in patients with psoriatic arthritis.**

Elkayam O, Ophir J, Brener S, Paran D, Wigler I, Efron D, Even-Paz Z, Politi Y, Yaron M.

**Source**



Department of Rheumatology, Tel Aviv Medical Center, Sackler Faculty of Medicine, University of Tel Aviv, Ichilov Hospital, Israel.

### **Abstract**

The purpose of this study was to evaluate the immediate and delayed effects of balneotherapy at the Dead Sea on patients with psoriatic arthritis (PsA). A total of 42 patients with PsA were treated at the Dead Sea for 4 weeks. Patients were randomly allocated into two groups: group 1 (23 patients) and group 2 (19 patients). Both groups received daily exposure to sun ultraviolet rays and regular bathing at the Dead Sea. Group 1 was also treated with mud packs and sulfur baths. Patients were assessed by a dermatologist and a rheumatologist 3 days before arrival, at the end of treatment, and at weeks 8, 16, and 28 from the start of treatment. The clinical indices assessed were morning stiffness, right and left hand grip, number of tender joints, number of swollen joints, Schober test, distance from finger to floor when bending forward, patient's self-assessment of disease severity, inflammatory neck and back pain and psoriasis area and severity index (PASI) score. Comparison between groups disclosed a similar statistically significant improvement for variables such as PASI, morning stiffness, patient self-assessment, right and left grip, Schober test and distance from finger to floor when bending forward. For variables such as tender and swollen joints, and inflammatory neck and back pain, improvement over time was statistically significant in group 1. Addition of mud packs and sulfur baths to sun ultraviolet exposure and Dead Sea baths seems to prolong beneficial effects and improves inflammatory back pain.

PMID: 10776684 [PubMed - indexed for MEDLINE]

### **Paper 21**

[Pharmacol Res Commun.](#) 1985 Jun;17(6):501-12.

### **Skin penetration of minerals in psoriatics and guinea-pigs bathing in hypertonic salt solutions.**

[Shani J](#), [Barak S](#), [Levi D](#), [Ram M](#), [Schachner ER](#), [Schlesinger T](#), [Robberecht H](#), [Van Grieken R](#), [Avrach WW](#).

### **Abstract**

Penetration of electrolytes through the human skin was measured in healthy volunteers and in psoriatic patients after bathing in the Dead-Sea or in simulated bath-salt solutions. Significant increases in the levels of serum Br, Rb, Ca and Zn were noticed only in the psoriatic patients after daily bathing in the Dead-Sea for a 4-week regimen. Guinea-pigs "bathed" in simulated Dead-Sea bath-salt solutions containing radionuclides of Ca, Mg, K and Br. Traces of each radionuclide were detected in the blood and in some internal organs after 60 minutes of bathing. The radionuclides showed a physiological pattern in their organ distribution. Even though the whole investigation was carried out in hypertonic solutions, there is a definite penetration of salts through healthy (human and guinea-pigs) and damaged (psoriatic) epidermis. This finding suggests that improvement of the psoriatic condition after bathing in the Dead-Sea, may be partly attributed (in addition to ultraviolet irradiation) to the minerals' effect on the psoriatic skin.

### **Paper 22**

[Pharmacology.](#) 1996 May;52(5):321-8.

## **Inhibition of proliferation of psoriatic and healthy fibroblasts in cell culture by selected Dead-sea salts.**

[Levi-Schaffer F](#), [Shani J](#), [Politi Y](#), [Rubinchik E](#), [Brenner S](#).

### **Source**

Department of Pharmacology, Hebrew University School of Pharmacy, Jerusalem, Israel.

### **Abstract**

The effect of five selected minerals abundant in the Dead-sea brine was studied on proliferation of fibroblasts grown from psoriatic and healthy skin biopsy specimens in cell culture. The reason for carrying out this study was looking for the mechanism of the antiproliferative effect of selective Dead-sea minerals in improving the psoriatic condition. Psoriatic skin shave biopsy specimens (both from involved and uninvolved areas of the body) as well as healthy skin (obtained from amputated limbs) were incubated in tissue culture, and their outgrowing fibroblasts were used for this study. The number of cells and their cyclic AMP content were used as parameters for cell division and for proving the selective involvement of magnesium salts in the antiproliferative effect. It is shown that the inhibitory effects of magnesium bromide and magnesium chloride on cell growth were significantly stronger than those of their corresponding potassium salts or of sodium chloride. These results were obtained with both psoriatic and healthy skin fibroblasts, indicating that the inhibitory effect of the selected Dead-sea minerals is present in healthy and psoriatic skin cells.

PMID: 8807676

[PubMed - indexed for MEDLINE]

### **Paper 23**

## **Penetration of selected Dead Sea minerals through a healthy rabbit skin, from a sustained-release transparent varnish, as a prospective treatment for psoriasis**

- [Jashovam Shani](#) <sup>a</sup>,
- [Ahmed Sulliman](#)<sup>a</sup>,
- [Itzhak Katzir](#)<sup>a</sup>,
- [Sarah Brenner](#)<sup>b</sup>

### **Abstract**

Bathing in the Dead Sea is an established treatment for psoriasis. Penetration of Dead Sea minerals into psoriatic skin is an effective factor in this treatment, but applying it clinically requires frequent bathing in the Dead Sea or in its bath-salt solution. We tested an ethyl-cellulose-based transparent varnish with a sustained-release property, for its penetrability of such minerals. Minerals tested were  $MgBr_2$  and  $KBr$ , known for their relevance in psoriatic proliferation. They were applied for up to three weeks. We could demonstrate that two weekly applications of the salt-containing varnish on healthy rabbit skin are enough to obtain elevated levels of magnesium and potassium in their plasma. We propose

the application of Dead Sea minerals containing varnish as a clinical treatment for psoriasis.

## Paper 28

### **Sulphurous medicinal waters increase somatostatin release: It is a possible mechanism of anti-inflammatory effect of balneotherapy in psoriasis**

Melinda Boros <sup>a</sup>, Ágnes Kemény <sup>a</sup>, Béla Sebők <sup>d</sup>, Teréz Bagoly <sup>a</sup>, Anikó Perkecz <sup>a</sup>, Zoltán Petőházi <sup>a</sup>, Gábor Maász <sup>b</sup>, János Schmidt <sup>b</sup>, László Márk <sup>b</sup>, Terézia László <sup>c</sup>, Zsuzsanna Helyes <sup>a</sup>, János Szolcsányi <sup>a</sup>, Erika Pintér <sup>a,\*</sup>

#### **Abstract**

*Aim:* Balneotherapy has been used in the treatment of immune-mediated skin diseases, but its molecular mechanism has yet to be elucidated. The aim of the present study was to observe the effect of sulphurous medicinal water in a murine dermatitis model and on psoriatic patients; moreover to investigate the role of hydrogen sulphide in the release of somatostatin during bathing treatment. *Materials and methods:* Inflammation was induced by oxazolone in the paw skin of mice. Oedema, TNF- $\alpha$  concentration, histological changes and myeloperoxidase level were investigated. Mice were bathed in medicinal water or distilled water for 20 min/day. To define the effect of hydrogen sulphide on somatostatin release mice were bathed in sodium hydrosulphide solution for 2 weeks. Somatostatin plasma concentration was detected by nanoHPLC-ESI-Q-TOF-MS. In the clinical study nineteen patients (PASI: 2.2–21.6) received 2  $\times$  25-min bath treatment for 21 days. Somatostatin-like immunoreactivity of the plasma was determined by radioimmunoassay. Before and after the balneotherapy skin biopsies were performed. *Results:* Oxazolone caused 29.43–33.73% paw swelling which was significantly reduced by the medicinal water. Myeloperoxidase, TNF- $\alpha$  levels and histological changes of the skin were unaltered. Somatostatin plasma concentration significantly increased in response to the bathing treatment. In the clinical study PASI markedly declined (0–13.4) and the plasma level of somatostatin increased significantly. Langerhans-cells migrated from the dermal pool to the epidermis. *Conclusion:* We conclude that balneotherapy is an effective treatment in psoriasis. Our results provided evidence that somatostatin released by H<sub>2</sub>S plays role in the mechanism of action of sulphurous medicinal water.

## Paper 29

### **Hydrogen sulfide impairs keratinocyte cell growth and adhesion inhibiting mitogen-activated protein kinase signaling**

Giuliana G, Francesca R, Malinverno C, Carubbi C, Pambianco M, de Panfilis G, Vitale M, Miranda P.

Laboratory Investigation (2009), 1–13

The effects of exogenous hydrogen sulfide (H<sub>2</sub>S) on normal skin-derived immortalized human keratinocytes have been investigated in detail. We show in vitro that exogenous hydrogen sulfide reduces clonal growth, cell proliferation and cell adhesion of human keratinocytes. H<sub>2</sub>S, in fact, decreases the frequency of the putative keratinocyte stem cell subpopulation in culture, consequently affecting clonal growth, and impairs cell proliferation and adhesion of mature cells. As a mechanistic explanation of these effects, we show at the molecular level that (i) H<sub>2</sub>S reduces the Raf/MAPK kinase/ERK signaling pathway; (ii) the reduced adhesion of sulfur-treated cells is associated to the downregulation of the expression of  $\alpha 4$ ,  $\alpha 2$  and  $\alpha 6$  integrins that are necessary to promote cell adhesion as well as anti-apoptotic and proliferative signaling in normal keratinocytes. One specific interest of the effects of sulfurs on keratinocytes derives from the potential applications of the results, as sulfur is able to penetrate the skin and a sulfur-rich balneotherapy has been known for long to be effective in the treatment of psoriasis. Thus, the relevance of our findings to the pathophysiology of psoriasis was tested in vivo by treating psoriatic lesions with sulfurs at a concentration comparable to that most commonly found in sulfurous natural springs. In agreement with the in vitro observations, the immunohistochemical analysis of patient biopsies showed a specific downregulation of ERK activation levels, the key molecular event in the sulfur-induced effects on keratinocytes.

#### **Paper 24**

Pharmacology. 1987;35(6):339-47.

#### **Effect of Dead-Sea brine and its main salts on cell growth in culture.**

Shani J, Sharon R, Koren R, Even-Paz Z.

Source: Department of Pharmacology, Hebrew University School of Pharmacy, Jerusalem, Israel.

#### **Abstract**

Diluted Dead-Sea brine and solutions of certain of its salts (chlorides and bromides of Na, K and Mg) were found to reversibly inhibit cell proliferation in culture. Bromides were more powerful as inhibitors than their chloride counterparts, and K salts were more effective than those of Na and Mg. KBr had the strongest inhibitory effect, which equalled that of diluted Dead-Sea brine at the same concentration. The favourable results of the Dead-Sea Spa treatment of psoriasis may thus be partly due to the penetration of minerals into the body, via the skin, with subsequent reinforcement of anti-proliferative mechanisms.

PMID:3432355[PubMed - indexed for MEDLINE]

#### **Paper 25**

[J Invest Dermatol](#). 2000 Oct;115(4):680-6.

#### **Magnesium ions inhibit the antigen-presenting function of human epidermal Langerhans cells in vivo and in vitro. Involvement of ATPase, HLA-DR, B7 molecules, and cytokines.**

[Schempp CM](#), [Dittmar HC](#), [Hummler D](#), [Simon-Haarhaus B](#), [Schulte-Mönting J](#), [Schöpf E](#), [Simon JC](#).

## Source

Department of Dermatology, University of Freiburg, Freiburg, Germany.  
schempp@haut.ukl.uni-freiburg.de

## Abstract

The combination of seawater baths and solar radiation at the Dead Sea is known as an effective treatment for patients with psoriasis and atopic dermatitis. Dead Sea water is particularly rich in magnesium ions. In this study we wished to determine the effects of magnesium ions on the capacity of human epidermal Langerhans cells to stimulate the proliferation of alloreactive T cells. Twelve subjects were exposed on four subsequent days on the volar aspects of their forearms to 5% MgCl<sub>2</sub>, 5% NaCl, ultraviolet B (1 minimal erythema dose), MgCl<sub>2</sub> + ultraviolet B, and NaCl + ultraviolet B. Epidermal sheets were prepared from punch biopsies and were stained for ATPase and HLA-DR. Compared with untreated skin, the number of ATPase+/HLA-DR+ Langerhans cells was significantly reduced after treatment with MgCl<sub>2</sub> ( $p = 0.0063$ ) or ultraviolet B ( $p = 0.0005$ ), but not after NaCl ( $p = 0.7744$ ). We next questioned whether this reduced expression of ATPase and HLA-DR on Langerhans cells bears a functional relevance. Six subjects were treated on four subsequent days with 5% MgCl<sub>2</sub>, ultraviolet B (1 minimal erythema dose), and MgCl<sub>2</sub> + ultraviolet B. Epidermal cell suspensions from treated and untreated skin were assessed for their antigen-presenting capacity in a mixed epidermal lymphocyte reaction with allogeneic naive resting T cells as responder cells. Treatment with MgCl<sub>2</sub>, similarly to ultraviolet B, significantly reduced the capacity of epidermal cells to activate allogeneic T cells ( $p = 0.0356$ ). Magnesium ions also suppressed Langerhans cells function when added to epidermal cell suspensions in vitro. The reduced antigen-presenting capacity of Langerhans cells after treatment with MgCl<sub>2</sub> was associated with a reduced expression by Langerhans cells of HLA-DR and costimulatory B7 molecules, and with a suppression of the constitutive tumor necrosis factor- $\alpha$  production by epidermal cells in vitro. These findings demonstrate that magnesium ions specifically inhibit the antigen-presenting capacity of Langerhans cells and may thus contribute to the efficacy of Dead Sea water in the treatment of inflammatory skin diseases.

PMID: 10998143

[PubMed - indexed for MEDLINE]

Free full text

## Paper 26

Gruner S, Zwirner A, Boonen H, Sonnichsen N. - Effect of treatment with salt from the Dead Sea (Tomesa therapy) on epidermal Langerhans cells - A clinical study. *Z Hautkr* 1990;65:1146-51.

[Z Hautkr](#). 1990 Dec;65(12):1146-51.

## [Effect of treatment with salt from the Dead Sea (Tomesa therapy) on epidermal Langerhans cells - a clinical study].

[Article in German]

[Gruner S](#), [Zwirner A](#), [Boonen H](#), [Sönnichsen N](#).

## Source

Hautklinik und Poliklinik des Bereichs Medizin (Charité), Humboldt-Universität zu Berlin.

## Abstract

Among the therapeutical modes of psoriasis, sea-water baths with salts from the Dead Sea in combination with ultraviolet light (Tomesa therapy) play an important part. In a previous paper, we showed that treatment of isolated murine skin with Tomesa salt solutions resulted in an irreversible decrease of ATPase-positive epidermal Langerhans' cells. Our present study is concerned with the treatment of healthy persons and psoriasis patients with baths containing Tomesa salts, which lead to reduced amounts of detectable Langerhans' cells in the epidermis, as well. Baths containing sodium chloride in comparable concentrations, however, were without effect at all. Our findings demonstrate that the antipsoriatic activity of Tomesa therapy is not only due to physical effects but may also be the result of definable pharmacological actions of the salts on skin cells.

PMID: 2087844

[PubMed - indexed for MEDLINE]

## Paper 27

Greiner J, Diezel W. Inflammation inhibiting effect of magnesium ions in contact eczema reactions. *Z Hautarzt* 1990;41:602-5.

[Hautarzt](#). 1990 Nov;41(11):602-5.

## [Inflammation-inhibiting effect of magnesium ions in contact eczema reactions].

[Article in German]

[Greiner J](#), [Diezel W](#).

Source

Universitäts-Hautklinik, Humboldt-Universität zu Berlin Charité.

Abstract

Water containing high concentrations of magnesium ions (e.g. Dead Sea water) is effective in the treatment of inflammatory skin diseases. Therefore, we examined the influence of Mg<sup>2+</sup> on inflammation in allergic contact dermatitis induced by 1-chloro-2,4-dinitrobenzene (DNCB) in BALB/c mice. Animals challenged with 0.125% DNCB in the presence of magnesium chloride (28% and 14%) demonstrated significantly less pronounced contact dermatitis (ear swelling) than did animals challenged with DNCB alone (p less than 0.001 and p less than 0.01). In mice challenged with DNCB in combination with sodium chloride (14%) there was no statistically significant difference in the degree of ear swelling. These results were borne out in 5 patients known to be allergic to nickel, in whom magnesium chloride but not sodium chloride, suppressed nickel sulphate-induced contact dermatitis.

PMID: 2276913

[PubMed - indexed for MEDLINE]

# Annex C

## MUSCULOSKELETAL SYSTEM

### Paper 1

Cochrane Database Syst Rev. 2007 Oct 17;(4):CD006864.

### **Balneotherapy for osteoarthritis.**

Verhagen AP, Bierma-Zeinstra SM, Boers M, Cardoso JR, Lambeck J, de Bie RA, de Vet HC.

### **Source**

Erasmus MC University Medical Centre, Dept of General Practice, PO Box 1738, Rotterdam, Netherlands, 3000 DR. a.verhagen@erasmusmc.nl

### **Abstract**

#### **BACKGROUND:**

Balneotherapy (or spa therapy, mineral baths) for patients with arthritis is one of the oldest forms of therapy. One of the aims of balneotherapy is to soothe the pain and as a consequence to relieve patients' suffering and make them feel well. In this update we included one extra study.

#### **OBJECTIVES:**

To assess the effectiveness of balneotherapy for patients with osteoarthritis (OA).

#### **SEARCH STRATEGY:**

We searched the following databases up to October 2006: EMBASE, PubMed, the Cochrane 'Rehabilitation and Related Therapies' Field database, PEDro, CENTRAL (Issue 3, 2006) and performed reference checking and communicated with authors to retrieve eligible studies.

#### **SELECTION CRITERIA:**

Randomised controlled trials (RCT) comparing balneotherapy with any intervention or no intervention. At least 90% of the patient population had to be diagnosed with OA.

#### **DATA COLLECTION AND ANALYSIS:**

Two authors independently assessed quality and extracted data. Disagreements were solved by consensus. In the event of clinical heterogeneity or lack of data we refrained from statistical pooling.

#### **MAIN RESULTS:**

Seven trials (498 patients) were included in this review. Two studies compared spa-treatment with no treatment. One study evaluated baths as an add-on treatment to home exercises and another compared thermal water from Cserkeszölő with tap water (placebo). Three studies evaluated sulphur or Dead

Sea baths with no treatment or mineral baths with tap water baths or no treatment. Only one of the trials performed an intention-to-treat analysis and two studies provided data to perform an intention-to-treat analysis ourselves. A 'quality of life' outcome was reported by one trial. We found: silver level evidence concerning the beneficial effects on pain, quality of life and analgesic intake of mineral baths compared to no treatment (SMD between 1.82 and 0.34). a statistically significant difference in pain and function of Dead Sea + sulphur versus no treatment, only at end of treatment (WMD 5.7, 95%CI 3.3 to 8.1), but not at 3 month follow-up (WMD 2.6, 95%CI -1.1 to 6.3). no statistically significant differences in pain or function at one or three months of Dead Sea baths versus no treatment (WMD 0.5, 95%CI -0.6 to 1.6) or at one or three months of sulphur baths versus no treatment (WMD 0.4, 95%CI -0.9 to 1.7). Adverse events were not measured in the included trials.

### **AUTHORS' CONCLUSIONS:**

We found silver level evidence ([www.cochranemsk.org](http://www.cochranemsk.org)) concerning the beneficial effects of mineral baths compared to no treatment. Of all other balneological treatments no clear effects were found. However, the scientific evidence is weak because of the poor methodological quality and the absence of an adequate statistical analysis and data presentation. Therefore, the noted "positive findings" should be viewed with caution.

### **Paper 2**

PMID: 17943920 [PubMed - indexed for MEDLINE]

J Rheumatol. 2008 Jun;35(6):1118-23. Epub 2008 May 1.

### **Balneotherapy for osteoarthritis. A cochrane review.**

Verhagen A, Bierma-Zeinstra S, Lambeck J, Cardoso JR, de Bie R, Boers M, de Vet HC.

### **Source**

Department of General Practice, Erasmus Medical Centre University, Rotterdam, The Netherlands. [a.verhagen@erasmusmc.nl](mailto:a.verhagen@erasmusmc.nl)

### **Abstract**

#### **OBJECTIVE:**

Balneotherapy (or spa therapy, mineral baths) for patients with arthritis is one of the oldest forms of therapy. We assessed effectiveness of balneotherapy for patients with osteoarthritis (OA).

#### **METHODS:**

We performed a broad search strategy to retrieve eligible studies, selecting randomized controlled trials comparing balneotherapy with any intervention or with no intervention. Two authors independently assessed quality and extracted data. Disagreements were solved by consensus. In the event of clinical heterogeneity or lack of data we refrained from statistical pooling.

#### **RESULTS:**

Seven trials (498 patients) were included in this review: one performed an intention-to-treat analysis, 2 provided data for our own analysis, and one reported a "quality of life" outcome. We found silver-level evidence of mineral baths compared to no treatment (effect sizes 0.34-1.82). Adverse events were not measured or found in included trials.



## **CONCLUSION:**

We found silver-level evidence concerning the beneficial effects of mineral baths compared to no treatment. Of all other balneological treatments, no clear effects were found. However, the scientific evidence is weak because of the poor methodological quality and the absence of an adequate statistical analysis and data presentation.

PMID: 18464302 [PubMed - indexed for MEDLINE]

## **Paper 3**

Clin Rheumatol. 2009 May;28(5):501-7. Epub 2009 Feb 19.

### **Short- and long-term therapeutic effects of thermal mineral waters in knee osteoarthritis: a systematic review of randomized controlled trials.**

Harzy T, Ghani N, Akasbi N, Bono W, Nejari C.

#### **Source**

Department of Rheumatology, Hassan II University Medical Centre, Fez, Morocco. t\_harzy@yahoo.fr

#### **Abstract**

The objective of the study was to evaluate short- and long-term therapeutic effectiveness of natural thermal mineral waters in patients with knee osteoarthritis (OA). We performed a systematic review of randomized controlled trials (RCTs) testing efficacy of thermal mineral water for treating patients with knee OA. Trials were identified by systematic searches of PubMed, Cochrane Central Register of Controlled trials, and Amed. We used the MeSH terms balneotherapy, balneology, and mineral water in combination with knee and osteoarthritis. Literature screening and data extraction were performed in duplicate. Nine RCTs satisfied the inclusion criteria, all published as full journal articles. Trial duration ranged from 10 to 24 weeks (median 15.33 +/- 5.56 weeks). The final sample included 493 patients who provided data at the ends of the studies. All interventions that were used in these trials found out an improvement in pain and functional capacity, which were sustained until week 24. No serious adverse events were reported to be associated with thermal mineral waters treatment. This work provide the most current and comprehensive review of the existing evidence of short- and long-term therapeutic effects of thermal mineral waters in knee OA. Additional RCTs with similar intervention comparisons and outcome measures, bigger sample size, and longer follow-up are required to confirm these results and to assess the biological effect of thermal mineral waters in patients with knee OA.

PMID: 19225707 [PubMed - indexed for MEDLINE]

## **Paper 4**

Cochrane Database Syst Rev. 2003;(4):CD000518.

### **Balneotherapy for rheumatoid arthritis.**

Verhagen AP, Bierma-Zeinstra SM, Cardoso JR, de Bie RA, Boers M, de Vet HC.

#### **Source**

Department of General Practice, Erasmus MC, P.O. Box 1738, 3000 DR Rotterdam, Netherlands.

## **Abstract**

### **BACKGROUND:**

Balneotherapy (spa therapy) for patients with arthritis is one of the oldest forms of therapy. One of the aims of balneotherapy is to soothe the pain, improve joint motion and as a consequence to relieve people' suffering and make them feel well.

### **OBJECTIVES:**

To perform a systematic review on the effectiveness of balneotherapy for rheumatoid arthritis.

### **SEARCH STRATEGY:**

Using the Cochrane search strategy, studies were found by screening: 1) The MEDLINE CD-ROM database from 1966 to June 2002 and 2) the database from the Cochrane 'Rehabilitation and Related Therapies' Field, the Pedro database up to June 2002. Also, 3) reference checking and 4) personal communications with authors was carried out to retrieve eligible studies. Date of the most recent literature search: June, 2002

### **SELECTION CRITERIA:**

Studies were eligible if they were randomised controlled trials (RCTs) comparing balneotherapy with any other intervention or with no intervention. Included participants all suffered from definite or classical rheumatoid arthritis (RA) as defined by the American Rheumatism Association Criteria (ARA) or by the criteria of Steinbrocker. At least one of the WHO/ILAR core set of endpoints for RA clinical trials had to be among the main outcome measures.

### **DATA COLLECTION AND ANALYSIS:**

The Delphi list was the criteria list used to assess the components of methodological quality. Two reviewers carried out quality assessment and data extraction of the studies. Disagreements were solved by consensus.

### **MAIN RESULTS:**

Six trials, representing 355 people, were included in this review. Most trials reported positive findings (the absolute improvement in measured outcomes ranged from 0 to 44%), but were methodologically flawed to some extent. A 'quality of life' outcome was reported by two trials. None of the trials performed an intention-to-treat analysis and only two performed a comparison of effects between groups. Pooling of the data was not performed; because of heterogeneity of the studies, multiple outcome measurements, and the overall data presentation was too scarce.

### **REVIEWER'S CONCLUSIONS:**

One cannot ignore the positive findings reported in most trials. However the scientific evidence is insufficient because of the poor methodological quality, the absence of an adequate statistical analysis, and the absence, for the patient, of most essential outcome measures (pain, self assessed function, quality of life). Therefore, the noted "positive findings" should be viewed with caution. Because of the methodological flaws an answer about the apparent effectiveness of balneotherapy cannot be provided at this moment. A large, methodological sound trial is needed.

## **Update of**

Cochrane Database Syst Rev. 2000;(2):CD000518.  
PMID: 14583923 [PubMed - indexed for MEDLINE]  
Cochrane Database Syst Rev. 2000;(2):CD000518.

## **Paper 5**

Musculoskeletal Care. 2012 Jul 16. doi: 10.1002/msc.1028. [Epub ahead of print]

# **The Effectiveness of Hydrotherapy in the Management of Rheumatoid Arthritis: A Systematic Review.**

Al-Qubaeissy KY, Fatoye FA, Goodwin PC, Yohannes AM.

## **Source**

Department of Health Professions, Manchester Metropolitan University, Manchester, UK.

## **Abstract**

### **BACKGROUND:**

Hydrotherapy is frequently indicated for the rehabilitation of patients with rheumatoid arthritis (RA); nevertheless, there has been inadequate appraisal of its effectiveness. The potential benefits of hydrotherapy for patients with RA are to improve and/or maintain functional ability and quality of life.

### **OBJECTIVES:**

The aim of this systematic review was to evaluate the effectiveness of hydrotherapy in the management of patients with RA.

### **METHOD:**

AMED, CINAHL, EMBASE, MEDLINE, PubMed, Science Direct and Web of Science were searched between 1988 and May 2011. Keywords used were rheumatoid arthritis, hydrotherapy, aquatic physiotherapy, aqua therapy and water therapy. Searches were supplemented with hand searches of references of selected articles. Randomized controlled trials were assessed for their methodological quality using the Physiotherapy Evidence Database (PEDro) scale. This scale ranks the methodological quality of a study scoring 7 out of 10 as 'high quality', 5-6 as 'moderate quality' and less than 4 as 'poor quality'.

### **RESULTS:**

Initially, 197 studies were identified. Six studies met the inclusion criteria for further analysis. The average methodological quality for all studies was 6.8 using the PEDro scale. Most of the studies reported favourable outcomes for a hydrotherapy intervention compared with no treatment or other interventions for patients with RA. Improvement was particularly noted in reducing pain, joint tenderness, mood and tension symptoms, and increasing grip strength and patient satisfaction with hydrotherapy treatment in the short term.

### **CONCLUSIONS:**

There is some evidence to suggest that hydrotherapy has a positive role in reducing pain and improving the health status of patients with RA compared with no or other interventions in the short term. However, the long-term benefit is

unknown. Further studies are needed. Copyright © 2012 John Wiley & Sons, Ltd.

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PMID: 22806987 [PubMed - as supplied by publisher]

Rheumatol Int. 2008 Dec;29(2):119-30. Epub 2008 Aug 27.

## **Paper 6**

### **The effectiveness of hydrotherapy in the management of fibromyalgia syndrome: a systematic review.**

McVeigh JG, McGaughey H, Hall M, Kane P.

#### **Source**

School of Health Sciences, Health and Rehabilitation Sciences Research Institute, University of Ulster, Newtownabbey, BT37 0QB, Northern Ireland, UK. j.mcveigh@ulster.ac.uk

#### **Abstract**

Hydrotherapy is often used in the treatment of fibromyalgia syndrome (FMS), however there has been limited evaluation of its effectiveness. The aim of this systematic review was therefore to examine the effectiveness of hydrotherapy in the management of FMS. AMED, BNI, CINAHL, The Cochrane Library, EMBASE, MEDLINE, ProQuest, PubMed, Science Direct and Web of Science were searched (1990-July 2006). Key words used 'fibromyalgia' and 'hydrotherapy', 'balneotherapy', 'aqua therapy', 'pool therapy', 'water therapy', 'swimming', 'hydrogalvanic', 'spa therapy', 'physiotherapy', 'physical therapy' and 'rehabilitation'. Searches were supplemented with hand searches of selected journals. Randomised controlled trials (RCTs) were assessed for methodological quality using the van Tulder scale. Ten RCTs met the inclusion criteria. Mean methodological quality was 4.5/9 on the van Tulder scale. Positive outcomes were reported for pain, health-status and tender point count. There is strong evidence for the use of hydrotherapy in the management of FMS.

PMID: 18751709 [PubMed - indexed for MEDLINE]

## **Paper 7**

J Epidemiol. 2010;20(1):2-12. Epub 2009 Oct 31.

### **Effectiveness of aquatic exercise and balneotherapy: a summary of systematic reviews based on randomized controlled trials of water immersion therapies.**

Kamioka H, Tsutani K, Okuizumi H, Mutoh Y, Ohta M, Handa S, Okada S, Kitayuguchi J, Kamada M, Shiozawa N, Honda T.

#### **Source**

Faculty of Regional Environment Science, Tokyo University of Agriculture, Tokyo, Japan. h1kamiok@nodai.ac.jp

#### **Abstract**

#### **BACKGROUND:**

The objective of this review was to summarize findings on aquatic exercise and balneotherapy and to assess the quality of systematic reviews based on randomized controlled trials.

### **METHODS:**

Studies were eligible if they were systematic reviews based on randomized clinical trials (with or without a meta-analysis) that included at least 1 treatment group that received aquatic exercise or balneotherapy. We searched the following databases: Cochrane Database Systematic Review, MEDLINE, CINAHL, Web of Science, JDream II, and Ichushi-Web for articles published from the year 1990 to August 17, 2008.

### **RESULTS:**

We found evidence that aquatic exercise had small but statistically significant effects on pain relief and related outcome measures of locomotor diseases (eg, arthritis, rheumatoid diseases, and low back pain). However, long-term effectiveness was unclear. Because evidence was lacking due to the poor methodological quality of balneotherapy studies, we were unable to make any conclusions on the effects of intervention. There were frequent flaws regarding the description of excluded RCTs and the assessment of publication bias in several trials. Two of the present authors independently assessed the quality of articles using the AMSTAR checklist.

### **CONCLUSIONS:**

Aquatic exercise had a small but statistically significant short-term effect on locomotor diseases. However, the effectiveness of balneotherapy in curing disease or improving health remains unclear.

PMID: 19881230 [PubMed - indexed for MEDLINE] **Free full text**

### **Paper 8**

Rheumatology (Oxford). 2009 Sep;48(9):1155-9. Epub 2009 Jul 16.

### **Efficacy of hydrotherapy in fibromyalgia syndrome--a meta-analysis of randomized controlled clinical trials.**

Langhorst J, Musial F, Klose P, Häuser W.

### **Source**

Department of Internal Medicine V (Complementary and Integrative Medicine), University of Duisburg-Essen, Kliniken Essen-Mitte, Essen, Germany.

### **Abstract**

#### **OBJECTIVE:**

To systematically review the efficacy of hydrotherapy in FM syndrome (FMS).

#### **METHODS:**

We screened MEDLINE, PsychInfo, EMBASE, CAMBASE and CENTRAL (through December 2008) and the reference sections of original studies and systematic reviews on hydrotherapy in FMS. Randomized controlled trials (RCTs) on the treatment of FMS with hydrotherapy (spa-, balneo- and thalassotherapy, hydrotherapy and packing and compresses) were analysed. Methodological quality was assessed by the van Tulder score. Effects were summarized using standardized mean differences (SMDs).

## RESULTS:

Ten out of 13 RCTs with 446 subjects, with a median sample size of 41 (range 24-80) and a median treatment time of 240 (range 200-300) min, were included into the meta-analysis. Only three studies had a moderate quality score. There was moderate evidence for reduction of pain (SMD -0.78; 95% CI -1.42, -0.13;  $P < 0.0001$ ) and improved health-related quality of life (HRQOL) (SMD -1.67; 95% CI -2.91, -0.43;  $P = 0.008$ ) at the end of therapy. There was moderate evidence that the reduction of pain (SMD -1.27; 95% CI -2.15, -0.38;  $P = 0.005$ ) and improvement of HRQOL (SMD -1.16; 95% CI -1.96, -0.36;  $P = 0.005$ ) could be maintained at follow-up (median 14 weeks).

## CONCLUSIONS:

There is moderate evidence that hydrotherapy has short-term beneficial effects on pain and HRQOL in FMS patients. There is a risk to over-estimate the effects of hydrotherapy due to methodological weaknesses of the studies and to small trials included in meta-analysis.

PMID: 19608724 [PubMed - indexed for MEDLINE] [Free full text](#)

## Paper 9

Rheumatology (Oxford). 2006 Jul;45(7):880-4. Epub 2006 Jan 31.

### **Spa therapy and balneotherapy for treating low back pain: meta-analysis of randomized trials.**

Pittler MH, Karagülle MZ, Karagülle M, Ernst E.

#### **Source**

Complementary Medicine, Peninsula Medical School, Universities of Exeter and Plymouth, 25 Victoria Park Road, Exeter EX2 4NT, UK. M.H.Pittler@exeter.ac.uk

#### **Abstract**

#### **OBJECTIVES:**

Low back pain is a major public health concern and complementary treatments are frequently used for this condition. The objective of this systematic review and meta-analysis was to assess the evidence for or against the effectiveness of spa therapy and balneotherapy for treating low back pain.

#### **METHODS:**

Systematic searches were conducted on Medline, Embase, Amed Cochrane Central, the UK National Research Register and ClinicalTrials.gov (all until July 2005). Hand searches were performed and experts contacted. Methodological quality was assessed using a standard scale.

#### **RESULTS:**

Five randomized clinical trials met all inclusion criteria. Quantitative data synthesis was performed. The data for spa therapy, assessed on a 100 mm visual analogue scale (VAS), suggest significant beneficial effects compared with waiting list control groups (weighted mean difference 26.6 mm, 95% confidence interval 20.4-32.8,  $n=442$ ) for patients with chronic low back pain. For balneotherapy the data, assessed on a 100 mm VAS, also suggest beneficial effects compared with control groups (weighted mean difference 18.8 mm, 95% confidence interval 10.3-27.3,  $n=138$ ).

## **CONCLUSIONS:**

Even though the data are scarce, there is encouraging evidence suggesting that spa therapy and balneotherapy may be effective for treating patients with low back pain. These data are not compelling but warrant rigorous large-scale trials.

PMID: 16449365 [PubMed - indexed for MEDLINE] **Free full text**

## **Paper 10**

Clin Rheumatol. 2009 May;28(5):501-7. Epub 2009 Feb 19.

### **Short- and long-term therapeutic effects of thermal mineral waters in knee osteoarthritis: a systematic review of randomized controlled trials.**

Harzy T, Ghani N, Akasbi N, Bono W, Nejjari C.

#### **Source**

Department of Rheumatology, Hassan II University Medical Centre, Fez, Morocco. t\_harzy@yahoo.fr

#### **Abstract**

The objective of the study was to evaluate short- and long-term therapeutic effectiveness of natural thermal mineral waters in patients with knee osteoarthritis (OA). We performed a systematic review of randomized controlled trials (RCTs) testing efficacy of thermal mineral water for treating patients with knee OA. Trials were identified by systematic searches of PubMed, Cochrane Central Register of Controlled trials, and Amed. We used the MeSH terms balneotherapy, balneology, and mineral water in combination with knee and osteoarthritis. Literature screening and data extraction were performed in duplicate. Nine RCTs satisfied the inclusion criteria, all published as full journal articles. Trial duration ranged from 10 to 24 weeks (median 15.33 +/- 5.56 weeks). The final sample included 493 patients who provided data at the ends of the studies. All interventions that were used in these trials found out an improvement in pain and functional capacity, which were sustained until week 24. No serious adverse events were reported to be associated with thermal mineral waters treatment. This work provide the most current and comprehensive review of the existing evidence of short- and long-term therapeutic effects of thermal mineral waters in knee OA. Additional RCTs with similar intervention comparisons and outcome measures, bigger sample size, and longer follow-up are required to confirm these results and to assess the biological effect of thermal mineral waters in patients with knee OA.

PMID: 19225707 [PubMed - indexed for MEDLINE]

## **Paper 11**

Int J Clin Pract. 2009 Jul;63(7):1068-84.

### **The therapeutic effect of balneotherapy: evaluation of the evidence from randomised controlled trials.**

Falagas ME, Zarkadoulia E, Rafailidis PI.

#### **Source**

Alfa Institute of Biomedical Sciences (AIBS), Athens, Greece. m.falagas@aibs.gr

#### **Abstract**

## **STUDY DESIGN:**

Systematic review.

## **SUMMARY OF BACKGROUND DATA:**

There is widespread popular belief that balneotherapy is effective in the treatment of various ailments.

## **METHODS:**

We searched PubMed (1950-2006), Scopus and Cochrane library for randomised controlled trials (RCTs), examining the clinical effect of balneotherapy (both as a solitary approach and in the context of spa) on various diseases.

## **RESULTS:**

A total of 203 potentially relevant articles were identified. In all, 29 RCTs were further evaluated; 22 of them (75.8%) investigated the use of balneotherapy in rheumatological diseases and eight osteoarthritis, six fibromyalgia, four ankylosing spondylitis, four rheumatoid arthritis and three RCTs (10.3%) in other musculoskeletal system diseases (chronic low back pain). In addition, three relevant studies focused on psoriasis and one on Parkinson's disease. A total of 1720 patients with rheumatological and other musculoskeletal diseases were evaluated in these studies. Balneotherapy did result in more pain improvement (statistically different) in patients with rheumatological diseases and chronic low back pain in comparison to the control group in 17 (68%) of the 25 RCTs examined. In the remaining eight studies, pain was improved in the balneotherapy treatment arm, but this improvement was statistically not different than that of the comparator treatment arm(s). This beneficial effect lasted for different periods of time: 10 days in one study, 2 weeks in one study, 3 weeks in one study, 12 weeks in 2 studies, 3 months in 11 studies, 16-20 weeks in one study, 24 weeks in three studies, 6 months in three studies, 40 weeks in one study and 1 year in one study.

## **CONCLUSION:**

The available data suggest that balneotherapy may be truly associated with improvement in several rheumatological diseases. However, existing research is not sufficiently strong to draw firm conclusions.

PMID: 19570124 [PubMed - indexed for MEDLINE]

## **Paper 12**

Therapie. 2001 Nov-Dec;56(6):675-84.

## **[Methodological reflections on 20 randomized clinical hydrotherapy trials in rheumatology].**

[Article in French]

Queneau P, Françon A, Graber-Duvernay B.

## **Source**

Service de Médecine Interne et Thérapeutique, Hôpital Bellevue, CHU de Saint Etienne, 42055 Saint Etienne, France.

## **Abstract**



The aim of this study was to estimate the level of scientific evidence contributed by randomized clinical trials in rheumatologic indication of spa therapy. A literature search was made of computer data banks, with analysis of 20 randomized hydrotherapy trials. On the 20 identified randomized hydrotherapy trials, four were carried out double-blind; nine included a comparison of inter-groups evolution. The indications assessed are chronic low back pain, osteoarthritis of the knee and hip joints, osteoarthritis of fingers, fibromyalgia, rheumatoid arthritis and psoriasis arthritis. The results suggest durable, persisting improvement several months after balneological care, in accordance with the following evaluation criteria: pain, handicap, quality of life, consumption of analgesics and of nonsteroidal anti-inflammatory drugs (NSAIDs). It was concluded that randomized evaluations, demonstrating a beneficial and prolonged clinical effect of balneologic treatments, exist in respect of the main indications for rheumatologic hydrotherapy. These results acknowledge the medical help given by hydrotherapy within the aforesaid parameters, to which may be added a reduction of the adverse gastrointestinal events of NSAIDs. Evaluation needs to be continued to clarify the medical benefit offered by rheumatologic hydrotherapy.

PMID: 11878090 [PubMed - indexed for MEDLINE]

### **Paper 13**

Forsch Komplementarmed Klass Naturheilkd. 2004 Feb;11(1):33-41.

### **[Balneotherapy and spa therapy of rheumatic diseases in Turkey: a systematic review].**

[Article in German]

Karagülle MZ, Karagülle M.

#### **Source**

Medizinische Ökologie und Hydroklimatologie, Medizinische Fakultät Istanbul der Universität Istanbul, Turkey. mzkaragulle@tnn.net

#### **Abstract**

##### **AIM:**

Turkey has a lot of thermal and mineral springs and is looking back on a still vivid tradition of spa therapy and balneotherapy, applied especially for the treatment of rheumatic diseases. This tradition is predominantly empiric and intuitive, however, it has assumed some important aspects of modern balneotherapeutic methods as well. This article is aimed at presenting the characteristics of traditional and modern balneological and spa therapy forms in Turkey.

##### **METHOD:**

The studies which have been conducted between 1990 and 2000 in different spas in Turkey on the efficacy and effectiveness of spa therapy and balneotherapy for rheumatic diseases have been searched and analyzed independent of their design. A descriptive evaluation of the studies was carried out.

##### **RESULTS:**

A total of 15 published studies have been found and analyzed. The investigations have been carried out in 8 different spa resorts in Turkey. In these studies the effectiveness and efficacy of different balneological and spa

therapies on a variety of rheumatic diseases (from osteoarthritis to fibromyalgia and from rheumatoid arthritis to low back pain) could be shown. Nearly all studied balneotherapeutic modalities were applied as bathing cures. Only in one study peloid therapy was applied. Balneotherapeutic therapy was applied in a modern and traditional way, and both open and stationary spa therapy forms were used at the same time.

### **CONCLUSIONS:**

The review has shown the effectiveness of the investigated spa therapy and balneotherapy forms. It could be concluded that nearly all forms of spa therapy and balneotherapy used for the treatment of rheumatic diseases in Turkey are effective. A definitive conclusion, however, is not possible because of the heterogeneity of the study designs, methodological flaws, and the publication bias. In future good quality randomized controlled trials are needed.

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PMID: 15004446 [PubMed - indexed for MEDLINE]

### **Paper 14**

Clin Ter. 2008 Sep-Oct;159(5):377-80.

### **[New evidences on spa therapy in fibromyalgia].**

[Article in Italian]

Giannitti C, Bellisai B, Iacoponi F, Petraglia A, Fioravanti A.

### **Source**

UOC di Reumatologia, Dipartimento di Medicina Clinica e Scienze Immunologiche, Università di Siena, Siena, Italia.

### **Abstract**

Spa therapy is one of the most commonly used non-pharmacological approaches for many rheumatic diseases. In Fibromyalgia Syndrome (FS) it may be useful for the chronic widespread musculoskeletal pain. Because of the unknown aetiology and the not clear understood pathogenesis, there is no standard therapy regimen for FS. Also the mechanisms of action of spa therapy are not completely known, but most probably the benefits could be derived from mechanical, physical and chemical factors. Muscle tone and pain intensity can be positively influenced by mud packs and thermal baths. The review of international data from 2000 to 2007 confirms that spa therapy should be a valid tool in the multidisciplinary approach of the Primary FS.

PMID: 18998040 [PubMed - indexed for MEDLINE]

### **Paper 15**

Rheumatology (Oxford). 2009 Sep;48(9):1155-9. Epub 2009 Jul 16.

### **Efficacy of hydrotherapy in fibromyalgia syndrome--a meta-analysis of randomized controlled clinical trials.**

Langhorst J, Musial F, Klose P, Häuser W.

### **Source**

Department of Internal Medicine V (Complementary and Integrative Medicine), University of Duisburg-Essen, Kliniken Essen-Mitte, Essen, Germany.

### **Abstract**

## **OBJECTIVE:**

To systematically review the efficacy of hydrotherapy in FM syndrome (FMS).

## **METHODS:**

We screened MEDLINE, PsychInfo, EMBASE, CAMBASE and CENTRAL (through December 2008) and the reference sections of original studies and systematic reviews on hydrotherapy in FMS. Randomized controlled trials (RCTs) on the treatment of FMS with hydrotherapy (spa-, balneo- and thalassotherapy, hydrotherapy and packing and compresses) were analysed. Methodological quality was assessed by the van Tulder score. Effects were summarized using standardized mean differences (SMDs).

## **RESULTS:**

Ten out of 13 RCTs with 446 subjects, with a median sample size of 41 (range 24-80) and a median treatment time of 240 (range 200-300) min, were included into the meta-analysis. Only three studies had a moderate quality score. There was moderate evidence for reduction of pain (SMD -0.78; 95% CI -1.42, -0.13;  $P < 0.0001$ ) and improved health-related quality of life (HRQOL) (SMD -1.67; 95% CI -2.91, -0.43;  $P = 0.008$ ) at the end of therapy. There was moderate evidence that the reduction of pain (SMD -1.27; 95% CI -2.15, -0.38;  $P = 0.005$ ) and improvement of HRQOL (SMD -1.16; 95% CI -1.96, -0.36;  $P = 0.005$ ) could be maintained at follow-up (median 14 weeks).

## **CONCLUSIONS:**

There is moderate evidence that hydrotherapy has short-term beneficial effects on pain and HRQOL in FMS patients. There is a risk to over-estimate the effects of hydrotherapy due to methodological weaknesses of the studies and to small trials included in meta-analysis.

PMID: 19608724 [PubMed - indexed for MEDLINE] [Free full text](#)

## **Paper 16**

Bull Acad Natl Med. 2009 Jun;193(6):1345-56; discussion 1356-8.

**[Spa therapy in rheumatology. Indications based on the clinical guidelines of the French National Authority for health and the European League Against Rheumatism, and the results of 19 randomized clinical trials].**

[Article in French]

Françon A, Forestier R.

## **Source**

Centre de recherches rhumatologiques et thermales, 73100 Aix les Bains. alain-francon@wanadoo.fr

## **Abstract**

The objective of this work was to update the rheumatologic indications of spa therapy, based on clinical practice guidelines published by the French National Authority for Health (HAS) and the European League Against Rheumatism (EULAR), and on the results of randomized clinical trials (RCT) **METHODOLOGY:** We first examined the indications for which spa therapy is mentioned and/or recommended in HAS and EULAR guidelines. We then

identified RCTs in spa therapy and rheumatology by using the key words spa therapy, balneology, balneotherapy, hydrotherapy, mud therapy and mineral water in the Pubmed, Pascal and Embase databases. Only RCTs including a statistical analysis of between-group outcomes were retained. We also examined the possible contribution of RCTs not listed in the bibliography of the guidelines.

## **RESULTS:**

## **RECOMMENDATIONS:**

spa therapy is recommended by HAS for chronic lower back pain, rank B and for stabilized rheumatoid arthritis, rank C. In ankylosing spondylitis, EULAR classifies spa therapy along with physiotherapy, rank A. In fibromyalgia, EULAR recommends hot-water balneology, an important component of spa therapy, rank B, based on five RCTs, of which three were carried out in thermal springs. Nineteen RCTs that comprised a statistical comparison of between-group outcomes were identified. Sixteen studies indicated a persistent improvement (at least twelve weeks) in pain, analgesic and non-steroidal antiinflammatory drug consumption, functional capacity and/or quality of life, in the following indications: chronic lower back pain, knee osteoarthritis, hand osteoarthritis, fibromyalgia, ankylosing spondylitis and rheumatoid arthritis (PR).

## **CONCLUSION:**

Spa therapy, or hot-water balneology, appears to be indicated for chronic low back pain, stabilized rheumatoid arthritis, ankylosing spondylitis and fibromyalgia. RCT findings suggest that patients with knee and hand osteoarthritis might also benefit.

PMID: 20120164 [PubMed - indexed for MEDLINE]

## **Paper 17**

J Rheumatol. 1997 Oct;24(10):1964-71.

## **Taking baths: the efficacy of balneotherapy in patients with arthritis. A systematic review.**

Verhagen AP, de Vet HC, de Bie RA, Kessels AG, Boers M, Knipschild PG.

### **Source**

Department of Epidemiology, Maastricht University, The Netherlands.

### **Abstract**

#### **OBJECTIVE:**

To review English, French, German, and Dutch language studies of the effectiveness of balneotherapy. Balneotherapy (hydrotherapy or spa therapy) is one of the oldest forms of therapy for patients with arthritis. One of the aims of balneotherapy is to relieve pain.

#### **METHODS:**

We performed a systematic review that included randomized and nonrandomized studies. Quality scores of the studies were determined using a criteria list.

#### **RESULTS:**

Most studies report positive findings, but all studies showed methodological flaws. A quality of life measurement was never reported as an outcome measure. None of the randomized clinical trials included intention-to-treat analysis or comparison of effects between groups.

## **CONCLUSION:**

Because of the methodological flaws a conclusion about the efficacy of balneotherapy cannot be provided from studies we reviewed. We conclude that most flaws found could be avoidable in future research.

PMID: 9330940 [PubMed - indexed for MEDLINE]

## **Paper 18**

Joint Bone Spine. 2008 Mar;75(2):138-48. Epub 2007 Dec 31.

## **Crenobalneotherapy for limb osteoarthritis: systematic literature review and methodological analysis.**

Forestier R, Françon A.

### **Source**

Aix-les-Bains Rheumatology and Spa Therapy Research Center, National Spas, Aix-les-Bains, France.

### **Abstract**

#### **OBJECTIVES:**

To conduct a systematic literature review on crenobalneotherapy for limb osteoarthritis and to discuss the study methods used to evaluate this treatment modality.

#### **METHODS:**

We searched Medline using the following keywords: "spa therapy", "mud", "radon", "balneotherapy", and "hydrotherapy" in combination with "osteoarthritis", "arthrosis", and "gonarthrosis". We also reviewed the reference lists of articles retrieved by the Medline search. Studies that compared crenobalneotherapy to any other intervention or to no intervention were selected, and a checklist was used to assess their internal validity. External validity and the quality of the statistical analysis were evaluated also.

#### **RESULTS:**

Crenobalneotherapy was associated with improvements in the evaluation criteria (pain, function, and quality of life) compared to baseline. However, inadequate internal validity precluded the establishment of a causal link between these improvements and crenobalneotherapy. External validity was often poorly defined. Some studies found no significant differences with the control group but failed to include a sample-size calculation, suggesting inadequate statistical power as a possible explanation for the result. In several studies, the use of multiple evaluation criteria and measurements led to a high risk of Type I error.

#### **CONCLUSION:**

Although the consistency of the results suggests a therapeutic effect of crenobalneotherapy in limb osteoarthritis, available studies are methodologically inadequate and sample sizes too small to allow definitive conclusions. We suggest a number of solutions to these shortcomings. Carefully designed studies

in larger patient populations are needed to determine the role of hydrotherapy in knee osteoarthritis.  
PMID: 18313346 [PubMed - indexed for MEDLINE]

## **Paper 19**

Musculoskeletal Care. 2012 Jul 16. doi: 10.1002/msc.1028. [Epub ahead of print]

# **The Effectiveness of Hydrotherapy in the Management of Rheumatoid Arthritis: A Systematic Review.**

Al-Qubaeissy KY, Fatoye FA, Goodwin PC, Yohannes AM.

## **Source**

Department of Health Professions, Manchester Metropolitan University, Manchester, UK.

## **Abstract**

### **BACKGROUND:**

Hydrotherapy is frequently indicated for the rehabilitation of patients with rheumatoid arthritis (RA); nevertheless, there has been inadequate appraisal of its effectiveness. The potential benefits of hydrotherapy for patients with RA are to improve and/or maintain functional ability and quality of life.

### **OBJECTIVES:**

The aim of this systematic review was to evaluate the effectiveness of hydrotherapy in the management of patients with RA.

### **METHOD:**

AMED, CINAHL, EMBASE, MEDLINE, PubMed, Science Direct and Web of Science were searched between 1988 and May 2011. Keywords used were rheumatoid arthritis, hydrotherapy, aquatic physiotherapy, aqua therapy and water therapy. Searches were supplemented with hand searches of references of selected articles. Randomized controlled trials were assessed for their methodological quality using the Physiotherapy Evidence Database (PEDro) scale. This scale ranks the methodological quality of a study scoring 7 out of 10 as 'high quality', 5-6 as 'moderate quality' and less than 4 as 'poor quality'.

### **RESULTS:**

Initially, 197 studies were identified. Six studies met the inclusion criteria for further analysis. The average methodological quality for all studies was 6.8 using the PEDro scale. Most of the studies reported favourable outcomes for a hydrotherapy intervention compared with no treatment or other interventions for patients with RA. Improvement was particularly noted in reducing pain, joint tenderness, mood and tension symptoms, and increasing grip strength and patient satisfaction with hydrotherapy treatment in the short term.

### **CONCLUSIONS:**

There is some evidence to suggest that hydrotherapy has a positive role in reducing pain and improving the health status of patients with RA compared with no or other interventions in the short term. However, the long-term benefit is

unknown. Further studies are needed. Copyright © 2012 John Wiley & Sons, Ltd.  
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PMID: 22806987 [PubMed - as supplied by publisher]

**Pittler MH, Karagülle MZ, Karagülle M, Ernst E.**

Spa therapy and balneotherapy for treating low back pain: meta-analysis of randomized trials.  
Rheumatology (Oxford). 2006 Jul;45(7):880-4. Epub 2006 Jan 31.

## **Paper 68**

Int J Biometeorol

DOI 10.1007/s00484-013-0667-6

Evidence-based hydro- and balneotherapy in Hungary—a systematic review and meta-analysis

T. Bender & G. Bálint & Z. Prohászka & P. Géher & I. K. Tefner

**Abstract** Balneotherapy is appreciated as a traditional treatment modality in medicine. Hungary is rich in thermal mineral waters. Balneotherapy has been in extensive use for centuries and its effects have been studied in detail. Here, we present a systematic review and meta-analysis of clinical trials conducted with Hungarian thermal mineral waters, the findings of which have been published by Hungarian authors in English. The 122 studies identified in different databases include 18 clinical trials. Five of these evaluated the effect of hydro- and balneotherapy on chronic low back pain, four on osteoarthritis of the knee, and two on osteoarthritis of the hand. One of the remaining seven trials evaluated balneotherapy in chronic inflammatory pelvic diseases, while six studies explored its effect on various laboratory parameters. Out of the 18 studies, 9 met the predefined criteria for meta-analysis. The results confirmed the beneficial effect of balneotherapy on pain with weight bearing and at rest in patients with degenerative joint and spinal diseases. A similar effect has been found in chronic pelvic inflammatory disease. The review also revealed that balneotherapy has some beneficial effects on antioxidant status, and on metabolic and inflammatory parameters.

Based on the results, we conclude that balneotherapy with Hungarian thermal-mineral waters is an effective remedy for lower back pain, as well as for knee and hand osteoarthritis.

## **Paper 69**

[Rheumatol Int.](#) 2013 May 21. [Epub ahead of print]

### **The effect of Neydharting mud-pack therapy on knee osteoarthritis: a randomized, controlled, double-blind follow-up pilot study.**

[Tefner IK](#), [Gaál R](#), [Koroknai A](#), [Ráthonyi A](#), [Gáti T](#), [Monduk P](#), [Kiss E](#), [Kovács C](#), [Bálint G](#), [Bender T](#).

Source

Józsefváros Municipal Health Service, Budapest, Hungary.

**Abstract**

The aim of this study was to evaluate the effects of Neydharting mud-pack therapy on the clinical parameters and quality of life in patients with knee

osteoarthritis. In this double-blind, randomized, follow-up study on 53 patients with knee osteoarthritis, one group received hot mud-pack therapy, whereas the other (control) group was treated with hot packs of a substance manufactured on 10 occasions for 2 weeks. Western Ontario and McMaster Universities Arthritis Index (WOMAC), EuroQoL-5D quality-of-life measure and need for analgesics and non-steroidal anti-inflammatory drugs were recorded before treatment, at the end of treatment (at Week 2), and at Weeks 6 and 12. The WOMAC and the EQ5D quality-of-life scores improved from the baseline to the end of treatment in both groups, and further improvement was observed during the follow-up period ( $p < 0.001$ , respectively, in both groups). The need for medications for knee joint pain improved in both groups, and these changes were significant only in the mud-treated group ( $p < 0.001$ ), but not in the control group ( $p = 0.106$ ) compared to baseline. The number of patients requiring medications for knee joint pain showed a continuous downward trend at the subsequent post-treatment visits by the mud-treated group, and these changes became significant by Visit 4 compared to baseline ( $p = 0.016$ ). The control group showed only temporary and not significant decrease. The difference was not significant between the groups in any of the outcome parameters at any visits. The Neydharting mud pack has a favorable effect on the clinical parameters, quality of life, and need for medications in patients with knee osteoarthritis. To evaluate the chemical effect, the number of patients should be increased.

## Paper 70

J. Cell. Physiol. 213: 826–833, 2007.

Exogenous hydrogen sulfide induces functional inhibition and cell death of cytotoxic lymphocytes subsets

PRISCO M, GOBBI G, SPONZILLI I, PAMBIANCO M, MALINVERNO C, CACCHIOLI A, DE PANFILIS G, VITALE M.

The toxic effects of exogenous hydrogen sulfide on peripheral blood lymphocytes have been investigated in detail. Hydrogen sulfide is now considered as a gasotransmitter with specific functional roles in different cell types, like neurons and vascular smooth muscle. Here we show that exogenous hydrogen sulfide induces a caspase-independent cell death of peripheral blood lymphocytes that depends on their intracellular glutathion levels, with a physiologically relevant subset specificity for CD8 $\beta$  T cells and NK cells. Although lymphocyte activation does not modify their sensitivity to HS, after 24 h exposure to hydrogen sulfide surviving lymphocyte subsets show a dramatically decreased proliferation in response to mitogens and a reduced IL-2 production. Overall, our data demonstrate that HS<sub>2</sub> reduces the cellular cytotoxic response of peripheral blood lymphocytes as well as their production of IL-2, therefore deactivating the major players of local inflammatory responses, adding new basic knowledge to the clinically well known anti-inflammatory effects of sulfur compounds.

## Paper 71

Laboratory Investigation (2006) 1–7

Hydrogen sulfide prevents apoptosis of human PMN via inhibition of p38 and caspase 3

Rinaldi L, Gobbi G, Pambianco M, Micheloni C, Mirandola P, Vitale M.

Hydrogen sulfide, together with carbon monoxide and nitric oxide, is now considered a gasotransmitter able to induce specific cellular responses. As hydrogen sulfide is a component of several natural compounds known to be effective in many inflammatory pathologies, particularly of the respiratory tract, we studied its effects in vitro on the survival and bactericidal activity of purified human neutrophils. We found that (1) HS<sup>-</sup> ions promote the survival of granulocytes, but not that of lymphocytes or eosinophils, cultured in serum-free



medium; (2) the pro-survival effect of HS is due to inhibition of caspase-3 cleavage and p38 MAP kinase phosphorylation; (3) the bactericidal activity of neutrophils is not impaired by hydrogen sulfide. We conclude that HS promotes the short-term survival of neutrophils potentially accelerating the resolution of inflammatory processes and preventing the occurrence of new ones.

## **Paper 20**

Cochrane Database Syst Rev. 2003;(4):CD000518.

### **Balneotherapy for rheumatoid arthritis.**

Verhagen AP, Bierma-Zeinstra SM, Cardoso JR, de Bie RA, Boers M, de Vet HC.

#### **Source**

Department of General Practice, Erasmus MC, P.O. Box 1738, 3000 DR Rotterdam, Netherlands.

#### **Abstract**

##### **BACKGROUND:**

Balneotherapy (spa therapy) for patients with arthritis is one of the oldest forms of therapy. One of the aims of balneotherapy is to soothe the pain, improve joint motion and as a consequence to relieve people' suffering and make them feel well.

##### **OBJECTIVES:**

To perform a systematic review on the effectiveness of balneotherapy for rheumatoid arthritis.

##### **SEARCH STRATEGY:**

Using the Cochrane search strategy, studies were found by screening: 1) The MEDLINE CD-ROM database from 1966 to June 2002 and 2) the database from the Cochrane 'Rehabilitation and Related Therapies' Field, the Pedro database up to June 2002. Also, 3) reference checking and 4) personal communications with authors was carried out to retrieve eligible studies. Date of the most recent literature search: June, 2002

##### **SELECTION CRITERIA:**

Studies were eligible if they were randomised controlled trials (RCTs) comparing balneotherapy with any other intervention or with no intervention. Included participants all suffered from definite or classical rheumatoid arthritis (RA) as defined by the American Rheumatism Association Criteria (ARA) or by the criteria of Steinbrocker. At least one of the WHO/ILAR core set of endpoints for RA clinical trials had to be among the main outcome measures.

##### **DATA COLLECTION AND ANALYSIS:**

The Delphi list was the criteria list used to assess the components of methodological quality. Two reviewers carried out quality assessment and data extraction of the studies. Disagreements were solved by consensus.

##### **MAIN RESULTS:**

Six trials, representing 355 people, were included in this review. Most trials reported positive findings (the absolute improvement in measured outcomes ranged from 0 to 44%), but were methodologically flawed to some extent. A

'quality of life' outcome was reported by two trials. None of the trials performed an intention-to-treat analysis and only two performed a comparison of effects between groups. Pooling of the data was not performed; because of heterogeneity of the studies, multiple outcome measurements, and the overall data presentation was too scarce.

### **REVIEWER'S CONCLUSIONS:**

One cannot ignore the positive findings reported in most trials. However the scientific evidence is insufficient because of the poor methodological quality, the absence of an adequate statistical analysis, and the absence, for the patient, of most essential outcome measures (pain, self assessed function, quality of life). Therefore, the noted "positive findings" should be viewed with caution. Because of the methodological flaws an answer about the apparent effectiveness of balneotherapy cannot be provided at this moment. A large, methodological sound trial is needed.

### **Update of**

Cochrane Database Syst Rev. 2000;(2):CD000518.  
PMID: 14583923 [PubMed - indexed for MEDLINE]

### **Paper 21**

Cochrane Database Syst Rev. 2000;(2):CD000518.

### **Balneotherapy for rheumatoid arthritis and osteoarthritis.**

Verhagen AP, de Vet HC, de Bie RA, Kessels AG, Boers M, Knipschild PG.

### **Source**

Department of General Practice, Erasmus University Rotterdam, P.O. Box 1738, 3000 DR Rotterdam, Netherlands. Verhagen@hag.fgg.eur.NL

### **Update in**

Cochrane Database Syst Rev. 2003;(4):CD000518.

### **Abstract**

#### **BACKGROUND:**

Balneotherapy (hydrotherapy or spa therapy) for patients with arthritis is one of the oldest forms of therapy. One of the aims of balneotherapy is to soothe the pain and as a consequence to relieve patients' suffering and make them feel well.

#### **OBJECTIVES:**

To perform a systematic review to assess the effects of balneotherapy for rheumatoid arthritis and osteoarthritis.

#### **SEARCH STRATEGY:**

Using the Cochrane search strategy, studies were found by screening: 1) The Medline CD-ROM database from 1966 to June 1999 and 2) the database from the Cochrane Field 'Rehabilitation and Related Therapies', which contains also studies published in journals not covered by Medline. Also, 3) reference checking and 4) personal communications with authors was carried out to retrieve eligible studies. To perform an adequate assessment of the

methodological quality the languages of the publications had to be: Dutch, English, French or German. Date of the most recent literature search: June, 1999

### **SELECTION CRITERIA:**

Studies were eligible if they were randomized controlled trials (RCT) comparing balneotherapy with any intervention or with no intervention. Patients included had rheumatoid arthritis (RA), osteoarthritis (OA) or some other form of arthritis. Trials incorporating patients with definite or classical rheumatoid arthritis (RA) as defined by the American Rheumatism Association Criteria (ARA) (Ropes 1958) (these criteria have changed over time) or by the criteria of Steinbrocker (1949) were regarded as a separate group. At least one of the WHO/ILAR core set of endpoints for RA clinical trials had to be the main outcome measures.

### **DATA COLLECTION AND ANALYSIS:**

A criteria list used to assess the methodological quality was the one developed at the Department of Epidemiology at the Maastricht University, called "the Maastricht list". The quality scores and data abstraction of the studies were carried out independently by two reviewers (HdV, RdB). Disagreements were solved by consensus.

### **MAIN RESULTS:**

Ten trials with 607 patients were included in this review. Most trials reported positive findings, but were methodologically flawed to some extent. A 'quality of life' outcome was reported by two trials. Just one of the randomized trials mentioned an intention-to-treat analysis and only three performed a comparison of effects between groups. Pooling of the data was not performed, because of heterogeneity of the studies, multiple outcome measurements, and, apart from two studies, the overall data presentation was too scarce to enable pooling of the data.

### **REVIEWER'S CONCLUSIONS:**

One cannot ignore the positive findings reported in most trials. However the scientific evidence is weak because of the poor methodological quality, the absence of an adequate statistical analysis, and the absence, for the patient, of most essential outcome measures (pain, quality of life). Therefore, the noted "positive findings" should be viewed with caution. Because of the methodological flaws an answer about the efficacy of balneotherapy cannot be provided at this time. Flaws found in the reviewed studies could be avoided in future trials.

PMID: 10796385 [PubMed - indexed for MEDLINE]

### **Paper 22**

Srp Arh Celok Lek. 2008 Jul-Aug;136(7-8):391-6.

### **[Beneficial effects of spa treatment on functional status and quality of life of patients with rheumatoid arthritis].**

[Article in Serbian]

Mustur D, Vesović-Potić V, Vujasinović-Stupar N, Ille T.

### **Abstract**

### **INTRODUCTION:**

Rheumatoid arthritis (RA) is a chronic constantly deteriorating disease of unpredictable clinical course, with exacerbations, remissions and damaged joints. It leads to the loss of self-sufficiency, independence in performing many daily activities, decrease of working ability and invalidity. Beside physical factors, which are regarded as most responsible for the poorer quality of life of RA patients, psychological changes are also significant, such as the feeling of helplessness, hopelessness and depression. The goal of the treatment of patients with RA is to decrease illness symptoms, slow down the development of illness progression, improvement of physical functioning and provision of expert help to the RA patients to adapt to life.

### **OBJECTIVE:**

The aim of the study was to assess the influence of spa therapy on the functional condition and life quality of RA patients.

### **METHODS:**

The study involved 69 patients with RA (51 female and 18 male, on average aged 55.2 +/- 11.4 years, with illness duration 12.5 +/- 7.5 years), and were a part of a cohort from Norway, suffering of inflammatory rheumatism. All the patients came for four-week rehabilitation at the Institute for Physical Medicine, Rehabilitation and Rheumatology "Dr. Simo Milosević" in Igalo, Montenegro. The RA patients underwent treatment with mud compresses, mud, mineral and pearl baths, as well as with underwater shower massage (balneotherapy) kinesitherapy and certain forms of electrotherapy with analgesic effects. The evaluation was done on admission and after completed physical therapy when we assessed RA patients' functional condition and quality of life. The functional condition was determined using the Modified Health Assessment Questionnaire (MHAQ), and the quality of life using the Medical Outcomes Study Short Form 36-item Questionnaire (SF-36), which encompassed eight life domains.

### **RESULTS:**

After completion of 28-dayspa therapy, RA patients showed a significant improvement in functional condition. Their quality of life was significantly improved in all dimensions of SF-36 Questionnaire ( $p < 0.01$ ), and the functional status (MHAQ score) was also significantly better ( $p < 0.01$ ).

### **CONCLUSION:**

Balneotherapy, together with climatic factors in Igalo, leads to a significant improvement of functional status and quality of life in patients suffering from RA. PMID: 18959175 [PubMed - indexed for MEDLINE]

### **Paper 23**

Srp Arh Celok Lek. 2009 Mar-Apr;137(3-4):171-4.

### **[Influence of balneophysical therapy on activity, functional capacity, and quality of life in patients with rheumatoid arthritis].**

[Article in Serbian]

Stojanović S, Dimić A, Stamenković B, Stanković A, Nedović J.

### **Abstract**

### **INTRODUCTION:**

It has been well known that balneophysical therapy has a therapeutic effect on clinical and biological parameters of disease activity in the patients with rheumatoid arthritis (RA).

### **OBJECTIVE:**

To determine the influence of balneophysical therapy on functional capacity, activity and quality of life of the patients with RA primarily treated with some of disease modifying antirheumatic drugs.

### **METHODS:**

The study enrolled 73 patients with RA treated with some of disease modifying antirheumatic drugs (Methotrexate in 85% of patients). During hospitalization at the Clinical Rheumatologic Department of the Institute "Niska Banja", the patients were treated, beside the medicamentous therapy, by hydrotherapy (oligomineral, homeothermic, low radioactive water), mineral peloid therapy, electrotherapy and kinesiotherapy. Before and after balneotherapy, the patients filled in the Health Assessment Questionnaire (HAQ) and the Quality of Life Rheumatoid Arthritis (QOL-RA) scale. The Disease Activity Score (DAS) 28 was used to measure the disease activity before and after balneotherapy. A possible value of HAQ was from 0 to 3, and QOL-RA from 0 to 10.

### **RESULTS:**

The mean value of the duration of balneophysical therapy was 14.7 +/- 4.8 days. We found significant improvement of functional capacity in the patients with RA. The average HAQ score before balneotherapy was 1.07 +/- 0.61, and 0.86 +/- 0.55 after balneotherapy, which was statistically significantly lower ( $p < 0.05$ ). DAS 28 after balneotherapy was also statistically significantly lower than DAS 28 before balneotherapy: the mean value of DAS 28 before therapy was 6.30 +/- 0.81 and after therapy 5.48 +/- 0.75 ( $p < 0.001$ ). The quality of life significantly improved after balneophysical therapy: the mean value of QOL-RA scale before therapy was 5.38 +/- 1.62 and after therapy 7.35 +/- 1.81 ( $p < 0.05$ ).

### **CONCLUSION:**

Balneophysical therapy, when properly dosed, is an effective, adjuvant therapy in the patients with RA of mild disease activity. Balneophysical therapy has a positive influence on disease activity, functional capacity and quality of life in the patients with rheumatoid arthritis.

PMID: 19459564 [PubMed - indexed for MEDLINE]

### **Paper 24**

Wiad Lek. 2006;59(1-2):72-7.

### **[Hydrogen sulphide water balneum effect on erythrocyte catalase activity in patients with rheumatoid arthritis--in vitro study].**

[Article in Polish]

Wozakowska-Kapton B, Grabski M, Kedziora J.

### **Source**

Zakładu Profilaktyki Chorób Układu Krążenia Zdrowiu Akademii Świętokrzyskiej w Kielcach.

### **Abstract**

The aim of the study was to investigate, in vitro, hydrogen sulphide water (HSW) balneum effect on erythrocyte catalase activity in patients with rheumatoid arthritis. Erythrocytes from twenty nine consecutive patients with rheumatoid arthritis (11 men, 18 women) aged 54 years were obtained. The control group comprised of 30 healthy subjects with a mean age of about 40 years. Patients with rheumatoid arthritis were subdivided into two groups twice: with active disease (18 patients) and in remission (11 patients), and secondly into patients receiving (21 subjects) and not receiving (8 subjects) non-steroidal anti-inflammatory drugs. For erythrocyte catalase activity evaluation, method of Beers and Sizer was used. Catalase activity was assessed after 5, 10, 15, and 20 minutes erythrocytes incubation with HSW. The mean baseline erythrocyte catalase activity (t0) was in rheumatoid arthritis patients of about 7.79 +/- 1.39 U/gHb and was significantly higher than in the control group: 6.96 +/- 2.68 U/gHb ( $p < 0.05$ ). After 5 minutes incubation with HSW (t5) erythrocyte catalase activity increased, in rheumatoid arthritis patients to 8.21 +/- 1.77 U/gHb, after 10 minutes (t10) was 8.14 +/- 2.25 U/gHb, in control group: 7.58 +/- 2.50 U/gHb and 7.68 +/- 3.22 U/gHb, respectively. However the difference was not statistically significant. After 20 minutes of incubation (t20) erythrocyte catalase activity was the highest in the patients with active rheumatoid arthritis (8.33 +/- 1.96 U/gHb) and differed significantly from the patients in remission (6.69 +/- 1.27 U/gHb) and from patients not receiving non-steroidal anti-inflammatory drugs (6.04 +/- 1.08 U/gHb). In rheumatoid arthritis patients erythrocyte catalase activity was higher when compared with control group and increased during incubation with HSW. It seems HSW balneum produce an antioxidant effect on erythrocyte status in patients with rheumatoid arthritis.

PMID: 16646297 [PubMed - indexed for MEDLINE]

## **Paper 25**

Rheumatol Int. 2005 Jan;25(1):49-54. Epub 2003 Nov 14.

### **Mud compress therapy for the hands of patients with rheumatoid arthritis.**

Codish S, Abu-Shakra M, Flusser D, Friger M, Sukenik S.

#### **Source**

Faculty of Health Sciences, Ben Gurion University of the Negev, Beer-Sheva, Israel.

#### **Abstract**

##### **OBJECTIVE:**

The aim of this study was to evaluate the efficacy of home treatment with mud compresses for the hands of patients with rheumatoid arthritis (RA).

##### **METHODS:**

Forty-five patients suffering from RA were enrolled in a double-blind, randomized, controlled study. Twenty-two were treated with true mud compresses (treatment group) and 23 were treated with attenuated mud compresses (control group). The compresses were applied in the patients' homes five times a week during a 3-week period. Patients were assessed four times: at baseline, upon completion of the 3-week treatment period, 1 month after the treatment, and 3 months after conclusion of the treatment period. Positive response was defined as reductions of 30% or more in the number of tender and swollen joints, 20% or more in physician global assessment of disease activity, and 20% or more in patient global assessment of the severity of joint pain.

## **RESULTS:**

In the treatment group, significant reductions in the number of swollen and tender joints and patients' global assessments of pain severity was observed at all post-treatment assessments. Significant improvement in the scores of physician global assessment was seen at the end of therapy and 1 month later. In the control group, no improvement in the number of swollen and tender joints or physician global assessment was found in any post-treatment evaluation. However, a significant reduction in patient global assessment of joint pain severity was reported at the end of therapy and 3 months after concluding treatment.

## **CONCLUSION:**

Treatment with mud compresses relieves pain affecting the hands and reduces the number of swollen and tender joints in the hands of patients suffering from RA. This treatment can augment conventional medical therapy in these patients. PMID: 14618372 [PubMed - indexed for MEDLINE]

## **Paper 26**

Musculoskeletal Care. 2012 Jul 16. doi: 10.1002/msc.1028. [Epub ahead of print]

## **The Effectiveness of Hydrotherapy in the Management of Rheumatoid Arthritis: A Systematic Review.**

Al-Qubaeissy KY, Fatoye FA, Goodwin PC, Yohannes AM.

### **Source**

Department of Health Professions, Manchester Metropolitan University, Manchester, UK.

### **Abstract**

#### **BACKGROUND:**

Hydrotherapy is frequently indicated for the rehabilitation of patients with rheumatoid arthritis (RA); nevertheless, there has been inadequate appraisal of its effectiveness. The potential benefits of hydrotherapy for patients with RA are to improve and/or maintain functional ability and quality of life.

#### **OBJECTIVES:**

The aim of this systematic review was to evaluate the effectiveness of hydrotherapy in the management of patients with RA.

#### **METHOD:**

AMED, CINAHL, EMBASE, MEDLINE, PubMed, Science Direct and Web of Science were searched between 1988 and May 2011. Keywords used were rheumatoid arthritis, hydrotherapy, aquatic physiotherapy, aqua therapy and water therapy. Searches were supplemented with hand searches of references of selected articles. Randomized controlled trials were assessed for their methodological quality using the Physiotherapy Evidence Database (PEDro) scale. This scale ranks the methodological quality of a study scoring 7 out of 10 as 'high quality', 5-6 as 'moderate quality' and less than 4 as 'poor quality'.

#### **RESULTS:**

Initially, 197 studies were identified. Six studies met the inclusion criteria for further analysis. The average methodological quality for all studies was 6.8 using the PEDro scale. Most of the studies reported favourable outcomes for a hydrotherapy intervention compared with no treatment or other interventions for patients with RA. Improvement was particularly noted in reducing pain, joint tenderness, mood and tension symptoms, and increasing grip strength and patient satisfaction with hydrotherapy treatment in the short term.

## **CONCLUSIONS:**

There is some evidence to suggest that hydrotherapy has a positive role in reducing pain and improving the health status of patients with RA compared with no or other interventions in the short term. However, the long-term benefit is unknown. Further studies are needed. Copyright © 2012 John Wiley & Sons, Ltd.

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PMID: 22806987 [PubMed - as supplied by publisher]

## **Paper 27**

Clin Rheumatol. 1992 Jun;11(2):243-7.

### **Mud pack therapy in rheumatoid arthritis.**

Sukenik S, Buskila D, Neumann L, Kleiner-Baumgarten A.

#### **Source**

Rheumatology Unit, Soroka Medical Center, Beer-Sheva, Israel.

#### **Abstract**

Twenty-eight patients with classical or definite rheumatoid arthritis were randomly divided into two groups of fourteen patients each. All patients were treated once a day with mud packs derived from the Dead Sea heated to 40 degrees C and applied over the four extremities, neck and back for 20 minutes. Group 1 was treated with the true mud packs and Group 2 with washed out and less concentrated mud packs. The study was double blind and of two weeks duration. All patients were evaluated by one rheumatologist both before treatment and two weeks later at the end of the treatment period. Follow-up evaluations were made one and three months after conclusion of the treatment. The clinical indices evaluated included duration of morning stiffness, hand-grip strength, activities of daily living, patient's own assessment of disease activity, number of active joints and the Ritchie index. A statistically significant improvement ( $p$  less than 0.01 or  $p$  less than 0.05) was observed in Group 1 only in most of the clinical indices, lasting between 1 to 3 months.

PMID: 1617901 [PubMed - indexed for MEDLINE]

## **Paper 28**

Ann Rheum Dis. 1990 Feb;49(2):99-102.

### **Sulphur bath and mud pack treatment for rheumatoid arthritis at the Dead Sea area.**

Sukenik S, Buskila D, Neumann L, Kleiner-Baumgarten A, Zimlichman S, Horowitz J.

#### **Source**



Rheumatology Unit, Soroka Medical Center, Ben-Gurion University of the Negev, Beer-Sheva, Israel.

### **Abstract**

Forty patients with classical or definite rheumatoid arthritis in a stage of active disease were treated for two weeks at a spa hotel. The patients were divided into four groups of 10. Group I was treated with daily mud packs, group II with daily hot sulphur baths, group III with a combination of mud packs and hot sulphur baths, and group IV served as a control group. The patients were assessed by a rheumatologist who was blinded to the treatment modalities. Statistically significant improvement for a period of up to three months was observed in the three treatment groups in most of the clinical indices. Improvement in the control group was minor in comparison and not statistically significant. No significant improvement was observed in any of the laboratory variables measured. Except for three mild cases of thermal reaction there were no side effects.

### **Comment in**

[Mineral bath therapy in arthritis. \[Ann Rheum Dis. 1991\]](#)  
PMID: 2180388 [PubMed - indexed for MEDLINE] PMID: PMC1003986

### **Paper 29**

Clin Exp Rheumatol. 1990 Jul-Aug;8(4):353-7.

### **Dead Sea bath salts for the treatment of rheumatoid arthritis.**

Sukenik S, Neumann L, Buskila D, Kleiner-Baumgarten A, Zimlichman S, Horowitz J.

### **Source**

Rheumatology Unit, Soroka Medical Center, Beer-Sheva, Israel.

### **Abstract**

Thirty patients with classical or definite rheumatoid arthritis were randomly divided into two groups of fifteen patients each of similar age, sex, duration and severity of disease, and medical treatment. All patients were treated once a day with bath salts heated to 35 degrees C for twenty minutes. Group I received Dead Sea bath salts and Group II, the control group, received sodium chloride (NaCl). The study was double-blind and of two weeks' duration. All patients were evaluated by one rheumatologist both before treatment, and two weeks later at the end of the treatment period. Follow-up evaluations were made one and three months after conclusion of the treatments. The clinical parameters evaluated included duration of morning stiffness, fifteen meter walk time, hand-grip strength, activities of daily living, circumference of proximal interphalangeal joints, number of active joints, Ritchie index and the patient's own assessment of disease activity. The laboratory parameters evaluated included erythrocyte sedimentation rate and serum levels of amyloid A, rheumatoid factor, sodium, potassium, calcium and magnesium. A statistically significant improvement (p less than 0.01 or p less than 0.05) was observed in Group I only, in most of the clinical parameters assessed. Maximal therapeutic effect was obtained at the end of the treatment and lasted up to one month.

PMID: 2397624 [PubMed - indexed for MEDLINE]

### **Paper 30**

Rheumatol Int. 2007 Oct;27(12):1157-61. Epub 2007 May 23.

#### **Effects of mud-bath treatment on fibromyalgia patients: a randomized clinical trial.**

Fioravanti A, Perpignano G, Tirri G, Cardinale G, Gianniti C, Lanza CE, Loi A, Tirri E, Sfriso P, Cozzi F.

#### **Source**

Department of Clinical Medicine and Immunological Sciences, University of Siena, Siena, Italy.

#### **Abstract**

The efficacy of balneotherapy in fibromyalgia syndrome (FS) has been well demonstrated, while controlled studies using mud packs are lacking. We performed a randomized clinical trial to evaluate the effects and the tolerability of mud-bath treatment in FS patients, who are poor responders to pharmacological therapy. Eighty patients with primary FS, according to ACR criteria, were randomly allocated to two groups: 40 were submitted to a cycle of 12 mud packs and thermal baths, and 40 were considered as controls. At baseline, after thermal treatment and after 16 weeks, patients were evaluated by FIQ, tender points count, VAS for "minor" symptoms, AIMS1 and HAQ. Control patients were assessed at the same time periods. A significant improvement of all evaluation parameters after mud-bath therapy and after 16 weeks was observed. Mud packs were well tolerated and no drop-outs were recorded. Our results suggest the efficacy and the tolerability of mud-bath treatment in primary FS.

PMID: 17520260 [PubMed - indexed for MEDLINE]

### **Paper 31**

J Back Musculoskelet Rehabil. 2011;24(1):57-65.

#### **The efficacy of balneotherapy and physical modalities on the pulmonary system of patients with fibromyalgia.**

Kesiktas N, Karagülle Z, Erdogan N, Yazıcıoğlu K, Yılmaz H, Paker N.

#### **Source**

Physical Medicine and Rehabilitation Department Istanbul University, Istanbul Medical Faculty, Istanbul, Turkey. nur.kesiktas@gmail.com

#### **Abstract**

Effects of balneotherapy on Primary Fibromyalgia Syndrome (FMS) have been studied well, except for its effect on the respiratory symptoms of FMS. In this study we allocated 56 patients with FMS into three groups who matched according to age, gender and duration of illness. All three groups received the same three physical therapy modalities (PTM): transcutaneous electrical nerve stimulation (TENS), ultrasound (US) and infrared (IR). The first group received PTM plus balneotherapy (PTM+BT), the second group received PTM alone (PTM), whilst the third group received PTM plus hydrotherapy (PTM+HT). All groups were treated for three weeks and in the same season. All patients were assessed at four time points: (a) at baseline, (b) on the 7th day of therapy, (c) at the end of therapy (after 3 weeks) and (d) at 6 months after the end of therapy. The effectiveness of treatments in all groups were evaluated in three main categories (pain, depressive and respiratory symptoms). Tender point count,

total algometric measurements and pain with visual analog scale for pain; Beck Depression Inventory (BDI) and Hamilton Depression Rating Scale (HDRS) for depression; dyspnea scale, and spirometric measurements for respiratory symptoms; plus quality of life with visual analog scale as a general measurement of effectiveness were taken at all four assessment time points. Both at the end of therapy and at the 6 months follow up significant improvements in dyspnea scale, and spirometric measurements, as well as in other measured parameters were observed in group PTM+BT. All groups achieved significant improvements in BDI and HDRS but scores of PTM and PTM+HT groups had overturned at 6 months follow up. Except second group which received PTM alone, pain evaluation assessments were improved at 6 month follow up in PTM+HT and PTM+BT groups. But PTM+BT group had more significant improvements at the end of therapy. PTM group had no significant change for dyspnea scale and spirometric measurements. PTM combined BT and HT groups achieved significant improvements at the end of therapies for dyspnea scale and spirometric measurements, but only PTM +BT group had significant improvements for dyspnea scale and spirometric measurements at six month follow up. The group of PTM+BT was significantly better than other groups. Our results suggest that supplementation of PTM with balneotherapy is effective on the respiratory and other symptoms of FMS and these effects were better than other protocols at 6 month follow up.  
PMID: 21248401 [PubMed - indexed for MEDLINE]

### **Paper 32**

Rheumatol Int. 2007 Mar;27(5):441-6.

### **Effects of balneotherapy on serum IL-1, PGE2 and LTB4 levels in fibromyalgia patients.**

Ardiç F, Ozgen M, Aybek H, Rota S, Cubukçu D, Gökgöz A.

#### **Source**

Department of Physical Medicine and Rehabilitation, Faculty of Medicine, Pamukkale University, Denizli, Turkey. fardic@pamukkale.edu.tr

#### **Abstract**

The purpose of this study was to investigate the clinical effects of balneotherapy in the treatment of Fibromyalgia Syndrome (FMS) and to determine if balneotherapy influences serum levels of inflammation markers, IL-1, PGE2 and LTB4. 24 primary fibromyalgia female patients diagnosed according to American College of Rheumatology criteria were included to the study. Their ages ranged between 33 and 55 years. FMS patients were randomly assigned in two groups as, group 1 (n = 12) and group 2 (n = 12). Group 1 received 20-min bathing, once in a day for five days per week. Patients participated in the study for 3 weeks (total of 15 sessions) in Denizli. Group 2 did not receive balneotherapy. FMS patients were evaluated by tenderness measurements (tender point count and algometry), Visual Analogue Scale, Beck's Depression Index, Fibromyalgia Impact Questionnaire. Ten healthy women recruited group three as the controls. Serum PGE2, LTB4 and IL1-alpha levels were measured in all three groups. The biochemical measurements and clinical assessments were performed before and at the end of general period of therapy. Statistically significant alterations in algometric score, Visual Analogue score, Beck's Depression Index and PGE2 levels (P < 0.001), numbers of tender points (P < 0.01) and Fibromyalgia Impact Questionnaire score (P < 0.05) were found after the balneotherapy between group 1 and 2. Mean PGE2 level of FMS patients were higher compared to healthy control group (P < 0.0001) and decreased after the treatment period, only in group 1 (P < 0.05). As in the group 2 and 3, detectable IL-1 and LTB4

measurements were insufficient, statistical analysis was performed, only in group 1. After balneotherapy IL-1 and LTB4 significantly decreased in group 1 ( $P < 0.05$ ). In conclusion, balneotherapy is an effective choice of treatment in patients with FMS relieving the clinical symptoms, and possibly influencing the inflammatory mediators.

PMID: 17033835 [PubMed - indexed for MEDLINE]

### **Paper 33**

Rheumatol Int. 2008 Dec;29(2):147-52. Epub 2008 Jul 4.

#### **Thalassotherapy for fibromyalgia: a randomized controlled trial comparing aquatic exercises in sea water and water pool.**

de Andrade SC, de Carvalho RF, Soares AS, de Abreu Freitas RP, de Medeiros Guerra LM, Vilar MJ.

#### **Source**

Division of Rheumatology, Department of Clinical Medicine, Postgraduate Program in Health Sciences, Federal University of Rio Grande do Norte, Natal, RN, Brazil. sandra.andrade.fisio@gmail.com

#### **Abstract**

The aim of this study was to evaluate the effectiveness of aerobic exercise in water pool compared with aerobic exercise performed in sea by women with fibromyalgia (FM). A total of 46 patients were randomly allocated into two groups: pool group (23 patients) and sea group (23 patients) that performed the same aerobic exercise program. Patients were evaluated baseline and after 12 weeks using: VAS, number of tender points, FIQ, SF-36, PSQI, and BDI. Both groups improved significantly in post-treatment for all the evaluated variables. There were no significant differences between two groups, except for BDI ( $F=2.418$ ,  $P<0.0001$ ). Aerobic exercise program performed in water (pool or sea) was effective for patients with FM. However, sea water exercises have been shown to bring more advantages related to emotional aspects. Then, exercise performed sea water (thalassotherapy) is an option for effective treatment with low cost for patients with FM.

PMID: 18600327 [PubMed - indexed for MEDLINE]

### **Paper 34**

Rheumatol Int. 2005 Dec;26(2):168-72. Epub 2005 Jun 17.

#### **SPA therapy in fibromyalgia: a randomised controlled clinic study.**

Dönmez A, Karagülle MZ, Tercan N, Dinler M, İşsever H, Karagülle M, Turan M.

#### **Source**

Department of Medical Ecology and Hydroclimatology, Istanbul Medical Faculty, Istanbul University, Istanbul, Turkey. donmeza@istanbul.edu.tr

#### **Abstract**

#### **OBJECTIVE:**

The aim of the present study is to evaluate the effectiveness of spa therapy in the management of fibromyalgia.

## **METHODS:**

Thirty women with fibromyalgia were randomly assigned to either a spa therapy group or a control group. The spa therapy group (n = 16) had spa treatment for 2 weeks in addition to their medical treatment. The control group (n = 14) continued to have their medical treatment and/or daily exercises. An investigator who was blinded for the intervention assessed all the patients for 9 months. Improvements in Fibromyalgia Impact Questionnaire (FIQ), pain and number of tender points were primary outcomes. Secondary outcome measures were improvement in sleep disturbance, fatigue, gastrointestinal symptoms, anxiety, Beck Depression Inventory and patient's global evaluation.

## **RESULTS:**

the spa group was found to be superior to the control group at the end of intervention in terms of FIQ, pain, tender point count, fatigue and patients' global assessment. This superiority remained for 6 months in FIQ, 1 month in pain and tender point count.

## **CONCLUSION:**

It was concluded that the addition of spa therapy to medical therapy has both short- and long-term beneficial effects in female patients with fibromyalgia.

PMID: 15965635 [PubMed - indexed for MEDLINE]

## **Paper 35**

Rheumatol Int. 2008 Dec;29(2):119-30. Epub 2008 Aug 27.

### **The effectiveness of hydrotherapy in the management of fibromyalgia syndrome: a systematic review.**

McVeigh JG, McGaughey H, Hall M, Kane P.

#### **Source**

School of Health Sciences, Health and Rehabilitation Sciences Research Institute, University of Ulster, Newtownabbey, BT37 0QB, Northern Ireland, UK. j.mcveigh@ulster.ac.uk

#### **Abstract**

Hydrotherapy is often used in the treatment of fibromyalgia syndrome (FMS), however there has been limited evaluation of its effectiveness. The aim of this systematic review was therefore to examine the effectiveness of hydrotherapy in the management of FMS. AMED, BNI, CINAHL, The Cochrane Library, EMBASE, MEDLINE, ProQuest, PubMed, Science Direct and Web of Science were searched (1990-July 2006). Key words used 'fibromyalgia' and 'hydrotherapy', 'balneotherapy', 'aqua therapy', 'pool therapy', 'water therapy', 'swimming', 'hydrogalvanic', 'spa therapy', 'physiotherapy', 'physical therapy' and 'rehabilitation'. Searches were supplemented with hand searches of selected journals. Randomised controlled trials (RCTs) were assessed for methodological quality using the van Tulder scale. Ten RCTs met the inclusion criteria. Mean methodological quality was 4.5/9 on the van Tulder scale. Positive outcomes were reported for pain, health-status and tender point count. There is strong evidence for the use of hydrotherapy in the management of FMS.

PMID: 18751709 [PubMed - indexed for MEDLINE]

## **Paper 36**

Isr Med Assoc J. 2005 Jul;7(7):443-6.

## **Spa therapy for ankylosing spondylitis at the Dead Sea.**

Codish S, Dobrovinsky S, Abu Shakra M, Flusser D, Sukenik S.

### **Source**

Department of Internal Medicine, Soroka University Medical Center, Beer Sheva, Israel.

### **Abstract**

#### **BACKGROUND:**

The efficacy of spa therapy in ankylosing spondylitis has not been investigated extensively.

#### **OBJECTIVE:**

To study the efficacy of balneotherapy and climatic therapy (climatotherapy) at the Dead Sea area in patients with ankylosing spondylitis.

#### **METHODS:**

In a single-blind randomized controlled study, 28 patients suffering from ankylosing spondylitis were allocated into two groups of 14 patients each. The first group (the combined treatment group) received balneotherapy (mud packs and sulfur pool) and exposure to the unique climatic conditions of the Dead Sea. The second group (the climatotherapy group) used the fresh water pool and experienced the same climatic conditions. The duration of treatment was 2 weeks and the follow-up period 3 months.

#### **RESULTS:**

For both patient groups a significant improvement was found in the outcome measures: Bath AS Disease Activity Index ( $P = 0.002$ ), VisualAnalog Scale for pain ( $P = 0.002$ ) and VAS for spinal movement ( $P = 0.011$ ). The variability was explained by the effect of time (within group effect) rather than the type of treatment (between group effect). Quality of life, assessed by the SF-36 questionnaire, was very low prior to the study, but improved in terms of pain amelioration in the combined treatment group.

#### **CONCLUSIONS:**

Climatotherapy at the Dead Sea area can improve the condition of patients suffering from long-standing ankylosing spondylitis.

PMID: 16011060 [PubMed - indexed for MEDLINE] **Free full text**

### **Paper 37**

Isr Med Assoc J. 1999 Oct;1(2):83-5.

## **Balneotherapy at the Dead Sea area for knee osteoarthritis.**

Sukenik S, Flusser D, Codish S, Abu-Shakra M.

### **Source**

Department of Rheumatology, Soroka Medical Center, Beer Sheva, Israel.  
ssukenik@bgumail.bgu.ac.il

## **Abstract**

### **BACKGROUND:**

Balneotherapy at the Dead Sea area has been applied in various inflammatory rheumatic diseases such as rheumatoid arthritis and psoriatic arthritis. The efficacy of balneotherapy at the Dead Sea area for the treatment of degenerative rheumatic diseases has not yet been formally evaluated.

### **OBJECTIVE:**

To evaluate the efficacy of balneotherapy at the Dead Sea area in patients suffering from osteoarthritis of the knees.

### **METHODS:**

Forty patients were randomly allocated into four groups of 10 patients. Group 1 was treated by bathing in a sulphur pool, group 2 by bathing in the Dead Sea, group 3 by a combination of sulphur pool and bathing in the Dead Sea, and group 4 served as the control group receiving no balneotherapy. The duration of balneotherapy was 2 weeks.

### **RESULTS:**

Significant improvement as measured by the Lequesne index of severity of osteoarthritis was observed in all three treatment groups, but not in the control group. This improvement lasted up to 3 months of follow-up in patients in all three treatment groups.

### **CONCLUSION:**

Balneotherapy at the Dead Sea area has a beneficial effect on patients with osteoarthritis of the knees, an effect that lasts at least 3 months.

PMID: 10731301 [PubMed - indexed for MEDLINE]

## **Paper 38**

Rheumatol Int. 2005 Apr;25(3):220-4. Epub 2004 Jul 15.

### **Hydrotherapy, balneotherapy, and spa treatment in pain management.**

Bender T, Karagülle Z, Bálint GP, Gutenbrunner C, Bálint PV, Sukenik S.

### **Source**

Polyclinic of Brother of St. John of God Hospitals, 7 Arpád fejedelem St, Budapest, Hungary 1025. bender@mail.datanet.hu

### **Abstract**

The use of water for medical treatment is probably as old as mankind. Until the middle of the last century, spa treatment, including hydrotherapy and balneotherapy, remained popular but went into decline especially in the Anglo-Saxon world with the development of effective analgesics. However, no analgesic, regardless of its potency, is capable of eliminating pain, and reports of life-threatening adverse reactions to the use of these drugs led to renewed interest in spa therapy. Because of methodologic difficulties and lack of research funding, the effects of 'water treatments' in the relief of pain have rarely been subjected to rigorous assessment by randomised, controlled trials. It is our opinion that the three therapeutic modalities must be considered separately, and this was done in the present paper. In addition, we review the research on the

mechanism of action and cost effectiveness of such treatments and examine what research might be useful in the future.

PMID: 15257412 [PubMed - indexed for MEDLINE]

### **Paper 39**

Rheumatol Int. 2011 Jan;31(1):1-8. Epub 2010 Dec 1.

## **Mechanisms of action of spa therapies in rheumatic diseases: what scientific evidence is there?**

Fioravanti A, Cantarini L, Guidelli GM, Galeazzi M.

### **Source**

Rheumatology Unit, Department of Clinical Medicine and Immunology, University of Siena, Viale Bracci 1, 53100 Siena, Italy. fioravanti7@virgilio.it

### **Abstract**

Spa therapy represents a popular treatment for many rheumatic diseases. The mechanisms by which immersion in mineral or thermal water or the application of mud alleviates suffering in rheumatic diseases are not fully understood. The net benefit is probably the result of a combination of factors, with mechanical, thermal and chemical effects among the most prominent ones. Buoyancy, immersion, resistance and temperature all play important roles.

According to the gate theory, pain relief may be due to the pressure and temperature of the water on skin; hot stimuli may influence muscle tone and pain intensity, helping to reduce muscle spasm and to increase the pain threshold. Mud-bath therapy increases plasma  $\beta$ -endorphin levels and secretion of corticotrophin, cortisol, growth hormone and prolactin. It has recently been demonstrated that thermal mud-pack therapy induces a reduction in the circulating levels of prostaglandin E2 (PGE2), leukotriene B4 (LTB4), interleukin-1 $\beta$  (IL-1 $\beta$ ) and tumour necrosis factor- $\alpha$  (TNF- $\alpha$ ), important mediators of inflammation and pain. Spa therapy has been found to cause an increase in insulin-like growth factor-1 (IGF1), which stimulates cartilage metabolism, and transforming growth factor- $\beta$  (TGF- $\beta$ ).

There is also evidence of the positive action of mud-packs and thermal baths on the oxidant/antioxidant system, with a reduction in the release of reactive oxygen (ROS) and nitrogen (RNS) species. Overall, thermal stress has an immunosuppressive effect. Many other non-specific factors may also contribute to the beneficial effects observed after spa therapy in some rheumatic diseases, including effects on cardiovascular risk factors, and changes in the environment, pleasant surroundings and the absence of work duties.

PMID: 21120502 [PubMed - indexed for MEDLINE]

### **Paper 40**

Rheumatol Int. 2012 Oct;32(10):3163-9. Epub 2011 Sep 27.

## **The effect of spa therapy in chronic low back pain: a randomized controlled, single-blind, follow-up study.**

Tefner IK, Németh A, Lászlófi A, Kis T, Gyetvai G, Bender T.

### **Source**

Józsefváros Health Care Services, Budapest, Hungary.

### **Abstract**



Effect of thermal water with high mineral content on clinical parameters and quality of life of patients with chronic low back pain was studied. In this randomized controlled, single-blind, follow-up study, 60 patients with chronic low back pain were randomized into two groups. The treatment group received balneotherapy with thermal-mineral water, and the control group bathed in tap water. Changes of the followings were evaluated: visual analogue scale (VAS) for pain, range of motion for the lumbar spine, Oswestry index, EuroQol-5D and Short Form-36 questionnaires. In the treatment group, the mobility of the lumbar spine, the Oswestry index, the VAS scores and the EuroQoL-5D index improved significantly. SF-36 items improved significantly in the treated group compared with baseline except for two parameters. Our study demonstrated the beneficial effect of balneotherapy with thermal mineral versus tap water on clinical parameters, along with improvements in quality of life.  
PMID: 21947373 [PubMed - in process]

## **Paper 41**

Forsch Komplementarmed Klass Naturheilkd. 2005 Aug;12(4):196-201. Epub 2005 Aug 29.

### **Effectiveness of balneotherapy in chronic low back pain -- a randomized single-blind controlled follow-up study.**

Balogh Z, Ordögh J, Gász A, Németh L, Bender T.

#### **Source**

Kehidakustány Health Spa, Kehidakustány, Budapest, Hungary.

#### **Abstract**

##### **OBJECTIVE:**

Balneotherapy, a domain of medical science, focuses on utilizing the beneficial effects of medicinal waters. Low back pain is among the most prevalent musculoskeletal disorders affecting a large proportion of the population during their lifetime. Although small in number, all controlled studies published on this subject have demonstrated the benefits of balneotherapy. This present study was undertaken to compare the effects of hydrotherapy with mineral water vs. tap water on low back pain.

##### **PATIENTS AND METHODS:**

A single-blind clinical study was carried out to appraise the therapeutic efficacy of reduced sulphurous water on 60 patients with low back pain. 30 subjects took baths in reduced sulphurous mineral water, whereas the other 30 patients used modified tap water of matching odor. Parameters determined at baseline, after balneo-/hydrotherapy, and at the end of the 3-month follow-up period included the results of the Visual Analogue Scale (VAS) score, the modified Oswestry index, mobility of the spine, antalgic posture, tenderness of the paravertebral muscles on palpation, the dose requirements for analgesics, and the efficacy assessed by the investigators and by the patients.

##### **RESULTS:**

Bathing in mineral water resulted in a statistically significant improvement. This was reflected by the VAS ( $p < 0.01$ ) and manifested by the mitigation of muscle spasm ( $p < 0.01$ ), the alleviation of local tenderness ( $p < 0.01$ ), the enhanced flexion-extension and rotation of the spine ( $p < 0.01$ ) as well as by the improvement of the Schober's index ( $p < 0.01$ ). All these beneficial changes

persisted as long as 3 months after the completion of balneotherapy. By contrast, hydrotherapy with tap water resulted only in the temporary improvement of just a single parameter: the VAS score improved significantly ( $p < 0.01$ ).

## **CONCLUSIONS:**

Balneotherapy in itself can alleviate low back pain. As demonstrated by this study, the analgesic efficacy and improvement of mobility accomplished by the use of mineral water is significantly superior to that afforded by hydrotherapy with tap water. Our results clearly establish the beneficial effects of mineral water. Moreover, it is a valuable adjunct to other forms of physical treatment as well as to pharmacotherapy.

PMID: 16137981 [PubMed - indexed for MEDLINE]

## **Paper 42**

South Med J. 2011 Aug;104(8):574-8.

### **Additional therapeutic effect of balneotherapy in low back pain.**

Dogan M, Sahin O, Elden H, Hayta E, Kaptanoglu E.

#### **Source**

Corum State Hospital, Clinic of Physical Medicine and Rehabilitation, Corum, Turkey.

#### **Abstract**

#### **OBJECTIVES:**

Balneotherapy has been widely used for treatment of chronic low back pain recently. However there are only a few clinical controlled trials on balneotherapy. The aim of the present study was to evaluate the effects of balneotherapy in patients with chronic low back pain.

#### **METHODS:**

Sixty patients with lumbar spondylosis were included in the study. In Group 1, patients received both balneotherapy and physiotherapy and in Group 2, patients received only physiotherapy for three weeks. The intensity of the pain was evaluated by Visual Analog Scale (VAS) and functional disability was scored according to Revised Oswestry Index (ROI). Spinal mobility was assessed by the Schober and lateral flexion tests. Variables were evaluated before and after the three weeks of treatment.

#### **RESULTS:**

The groups were comparable regarding age ( $P = 0.970$ ) and sex ( $P = 0.357$ ). There was no statistically significant difference between the two groups for baseline VAS ( $P = 0.838$ ), Schober test ( $P = 0.226$ ), and right ( $P = 0.642$ ) and left ( $P = 0.674$ ) lateral flexion measurements, and ROI scores ( $P = 0.798$ ). At the end of the therapy, all clinical parameters significantly improved in patients in both of the groups ( $P < 0.05$ ). VAS, Schober test, and ROI scores after the therapy were clearly superior in Group 1 in comparison to Group 2 ( $P < 0.05$ ).

#### **CONCLUSION:**

The results of the present study reiterate that besides conventional physiotherapy, balneotherapy may be effective in the treatment of patients with chronic low back pain.

PMID: 21886066 [PubMed - indexed for MEDLINE]

### **Paper 43**

Bull Acad Natl Med. 2009 Jun;193(6):1345-56; discussion 1356-8.

### **[Spa therapy in rheumatology. Indications based on the clinical guidelines of the French National Authority for health and the European League Against Rheumatism, and the results of 19 randomized clinical trials].**

[Article in French]

Françon A, Forestier R.

### **Source**

Centre de recherches rhumatologiques et thermales, 73100 Aix les Bains. alain-francon@wanadoo.fr

### **Abstract**

The objective of this work was to update the rheumatologic indications of spa therapy, based on clinical practice guidelines published by the French National Authority for Health (HAS) and the European League Against Rheumatism (EULAR), and on the results of randomized clinical trials (RCT) **METHODOLOGY:** We first examined the indications for which spa therapy is mentioned and/or recommended in HAS and EULAR guidelines. We then identified RCTs in spa therapy and rheumatology by using the key words spa therapy, balneology, balneotherapy, hydrotherapy, mud therapy and mineral water in the Pubmed, Pascal and Embase databases. Only RCTs including a statistical analysis of between-group outcomes were retained We also examined the possible contribution of RCTs not listed in the bibliography of the guidelines.

### **RESULTS:**

### **RECOMMENDATIONS:**

spa therapy is recommended by HAS for chronic lower back pain, rank B and for stabilized rheumatoid arthritis, rank C. In ankylosing spondylitis, EULAR classifies spa therapy along with physiotherapy, rank A. In fibromyalgia, EULAR recommends hot-water balneology, an important component of spa therapy, rank B, based on five RCTs, of which three were carried out in thermal springs. Nineteen RCTs that comprised a statistical comparison of between-group outcomes were identified Sixteen studies indicated a persistent improvement (at least twelve weeks) in pain, analgesic and non-steroidal antiinflammatory drug consumption, functional capacity and/or quality of life, in the following indications: chronic lower back pain, knee osteoarthritis, hand osteoarthritis, fibromyalgia, ankylosing spondylitis and rheumatoid arthritis (PR).

### **CONCLUSION:**

Spa therapy, or hot-water balneology, appears to be indicated for chronic low back pain, stabilized rheumatoid arthritis, ankylosing spondylitis and

fibromyalgia. RCT findings suggest that patients with knee and hand osteoarthritis might also benefit.  
PMID: 20120164 [PubMed - indexed for MEDLINE]

#### **Paper 44**

Vojnosanit Pregl. 2010 Jul;67(7):573-8.

### **Oxidative stress, hemoglobin content, superoxide dismutase and catalase activity influenced by sulphur baths and mud packs in patients with osteoarthritis.**

Jokić A, Sremcević N, Karagülle Z, Pekmezović T, Davidović V.

#### **Source**

Specialized Hospital for Rehabilitation, Banja Koviljaca Spa, Serbia.  
jokic71@gmail.com

#### **Abstract**

##### **BACKGROUND/AIM:**

It is well-known that sulphur baths and mud packs demonstrate beneficial effects on patients suffering from degenerative knee and hip osteoarthritis (OA) through the increased activity of protective antioxidant enzymes. The aim of this study was to assess lipid peroxidation level, i.e., malondialdehyde concentration, in individuals with knee and/or hip osteoarthritis (OA), as well as to determine the influence of sulphur baths and mud packs application on the activity of superoxide dismutase (SOD) and catalase (CAT) in order to minimize or eliminate excessive free radical species production (oxidative stress).

##### **METHODS:**

Thirty one patients with knee and/or hip OA of both sexes were included in the study. All OA patients received mud pack and sulphur bath for 20 minutes a day, for 6 consecutive days a week, over 3 weeks. Blood lipid peroxidation, i.e., malondialdehyde concentration, superoxide dismutase and catalase activity were measured spectrophotometrically, before, on day 5 during the treatment and at the end of spa cure. Healthy volunteers (n=31) were the controls.

##### **RESULTS:**

The sulphur baths and mud packs treatment of OA patients caused a significant decrease in plasma malondialdehyde concentration compared to the controls ( $p < 0.001$ ). The mean SOD activity before the therapy was 1836.24 U/gHb, on day 5 it rose to 1942.15 U/gHb and after the spa cure dropped to 1745.98 U/gHb. Catalase activity before the therapy was 20.56 kU/gHb and at the end of the therapy decreased to 16.16 kU/gHb. The difference in catalase activity before and after the therapy was significant ( $p < 0.001$ ), and also significant as compared to control ( $p < 0.001$ ). At the end of the treatment significant increase of hemoglobin level and significant decrease of pain intensity were noticed.

##### **CONCLUSION:**

A combined 3-week treatment by sulphur bath and mud packs led to a significant decrease of lipid peroxidation in plasma, as well as pain intensity in the patients with OA. These changes were associated with changes in plasma activity of SOD and CAT and a significant increase of hemoglobin level suggesting their role in beneficial effect of spa therapy in the patients with OA.

PMID: 20707053 [PubMed - indexed for MEDLINE]

### **Paper 45**

Rheumatol Int. 2010 Apr;30(6):739-47. Epub 2009 Jul 9.

## **Effect of balneotherapy on temporospatial gait characteristics of patients with osteoarthritis of the knee.**

Kiliçoğlu O, Dönmez A, Karagülle Z, Erdoğan N, Akalan E, Temelli Y.

### **Source**

Department of Orthopedics and Traumatology, Istanbul University, Istanbul Medical School, Millet Cad. 118, Fatih, 34093, Istanbul, Turkey. kilicoglu@istanbul.edu.tr

### **Abstract**

Effects of balneotherapy on gait properties of patients with osteoarthritis of the knee were investigated prospectively. A total of 30 patients with knee osteoarthritis received balneotherapy consisting of two daily thermomineral water baths for 2 weeks. Patients were evaluated using gait analysis and clinical scores, both within 2 weeks, before and after spa treatment. Patients were walking faster in their control analyses (0.81 +/- 0.21 to 0.89 +/- 0.19 m/s; P = 0.017), with a shorter mean stance time (63.0 +/- 3.3 to 61.8 +/- 2.5% stride; P = 0.007), an increased cadence (96 +/- 13.1 to 100 +/- 11.9 steps/min; P = 0.094) and stride length (996 +/- 174 to 1,058 +/- 142 mm; P = 0.017). Balneotherapy also resulted in a significant decrease in Lequesne knee osteoarthritis index (12.1 +/- 3.7 to 10.0 +/- 3.3 points; P = 0.003), VAS for pain (58 +/- 25 to 33 +/- 15; P = 0.0001), VAS for patients' (56 +/- 24 to 29 +/- 19; P < 0.001) and investigator's global assessment (55 +/- 20 to 26 +/- 15; P < 0.0001) and WOMAC score (2.1 +/- 0.7 to 1.6 +/- 0.8; P = 0.0004). Balneotherapy has positive effects on gait properties and clinical health quality parameters of patients with knee osteoarthritis in short-term evaluations.

PMID: 19588141 [PubMed - indexed for MEDLINE]

### **Paper 46**

Clin Rheumatol. 2007 Dec;26(12):2063-71. Epub 2007 Apr 13.

## **A 10-day course of SPA therapy is beneficial for people with severe knee osteoarthritis. A 24-week randomised, controlled pilot study.**

Karagülle M, Karagülle MZ, Karagülle O, Dönmez A, Turan M.

### **Source**

Department of Medical Ecology and Hydroclimatology, Istanbul Medical Faculty, University of Istanbul, Millet cad. 126, 34093, Istanbul, Turkey. mkaragulle@tnn.net

### **Abstract**

The objective of this study was to test if spa therapy can play a role in the management of severe knee osteoarthritis (OA). Twenty patients with radiologically and clinically severe knee OA were randomly assigned into spa and drug therapy groups. Spa group (n = 10) traveled to a spa town and stayed at a hotel for a 10-day spa therapy course. They followed a balneotherapy regimen including thermal pool baths at 37 degrees C for 20 min two times daily.

Drug therapy group (n = 10) stayed at home and followed their individually prescribed drug therapy (NSAIDs and paracetamol).

Patients were assessed at baseline (week 0), after spa therapy at 2 weeks (week 2) and during follow-up period at 12 (week 12) and 24 (week 24) weeks by a blinded investigator. Patients assessed with Lequesne algofunctional index (LAFI), pain (visual analogue scale, VAS), patient's and investigator's global evaluation (VAS), ten-stairs stepping up and down time, 15 m walking time and three times squatting up and down time.

Significant improvement in pain and LAFI scores were found at week 2, week 12 and week 24 in the spa therapy group compared to baseline. Comparing the two group differences, spa therapy was superior to drug therapy in pain reduction and in physician's global assessment at all time points. This superiority was also found in LAFI scores and patients' global assessments at week 12 and week 24. A 10-day course of spa therapy may be beneficial in short- and medium-term up to 24 weeks by reducing pain and improving functional status and overall well-being in patients with severe knee OA and may be considered as an effective therapeutic tool for such patients in countries like Turkey where it is widely available and (at least partly) reimbursed.

PMID: 17431728 [PubMed - indexed for MEDLINE]

## **Paper 47**

Ann Rheum Dis. 2010 Apr;69(4):660-5. Epub 2009 Sep 3.

### **Spa therapy in the treatment of knee osteoarthritis: a large randomised multicentre trial.**

Forestier R, Desfour H, Tessier JM, Françon A, Foote AM, Genty C, Rolland C, Roques CF, Bosson JL.

#### **Source**

Clinical Research Centre, CHU de Grenoble BP 217, Grenoble, France.

#### **Abstract**

##### **OBJECTIVE:**

To determine whether spa therapy, plus home exercises and usual medical treatment provides any benefit over exercises and usual treatment, in the management of knee osteoarthritis.

##### **METHODS:**

Large multicentre randomised prospective clinical trial of patients with knee osteoarthritis according to the American College of Rheumatology criteria, attending French spa resorts as outpatients between June 2006 and April 2007. Zelen randomisation was used so patients were ignorant of the other group and spa personnel were not told which patients were participating. The main endpoint criteria were patient self-assessed. All patients continued usual treatments and performed daily standardised home exercises. The spa therapy group also received 18 days of spa therapy (massages, showers, mud and pool sessions). MAIN ENDPOINT: The number of patients achieving minimal clinically important improvement (MCII) at 6 months, defined as  $\geq 19.9$  mm on the visual analogue pain scale and/or  $\geq 9.1$  points in a normalised Western Ontario and McMaster Universities osteoarthritis index function score and no knee surgery.

##### **RESULTS:**

The intention to treat analysis included 187 controls and 195 spa therapy patients. At 6 months, 99/195 (50.8%) spa group patients had MCII and 68/187

(36.4%) controls ( $\chi^2=8.05$ ;  $df=1$ ;  $p=0.005$ ). However, no improvement in quality of life (Short Form 36) or patient acceptable symptom state was observed at 6 months.

## **CONCLUSION:**

For patients with knee osteoarthritis a 3-week course of spa therapy together with home exercises and usual pharmacological treatments offers benefit after 6 months compared with exercises and usual treatment alone, and is well tolerated.

PMID: 19734131 [PubMed - indexed for MEDLINE] PMID: PMC2927613

**Free PMC Article**

## **Paper 48**

Therapie. 2012 Jan-Feb;67(1):43-8. Epub 2012 Apr 11.

## **[Sulphur Mineral Water and SPA Therapy in Osteoarthritis].**

[Article in French]

Costantino M, Filippelli A, Quenau P, Nicolas JP, Coiro V.

## **Source**

Association à but non lucratif F.I.R.S.Thermae (Formation interdisciplinaire, Recherches et Sciences Thermales), Division Médecine Thermale « Impresa A. Minieri - Terme di Telesse », Benevento, Italie - École en Hydrologie Médicale, Université de Parma, Italie.

## **Abstract**

**Objective.** Osteoarthritis (OA), the most common degenerative osteoarticular disease, is cause of pain and limitations in physical function with high disability that can conduct to a state of psychological stress, not always considered adequately, with negative impact on the quality of life. The mud and bath therapy can improve this aspect. However, these studies are insufficient. The objective of our research was to evaluate the impact of SPA therapy cycle on safety, efficacy and psychosocial disability in osteoarthritis. **Materials and methods.** The study was carried out on 99 subjects suffering from OA. The patients has treated for 12 days with applications of sulphurous mud-bath therapy from "Terme di Telesse" (Benevento, Italy). At the beginning and at the end of the SPA therapy considered has assessed: 1) the adverse reactions; 2) the efficacy on the pain and functional limitations; c) the impact on the psychosocial function using the VAS scale, the SF-36 questionnaire, the WOMAC index and the SDS-Zung test. Statistical analysis of the data was performed by determining the mean  $\pm$  SD. The results were compared with the Student "t" test or Wilcoxon test. A p value < 0.05 was considered significant. **Results.** In comparison to the basal values, this investigation has demonstrated that sulphurous mud and bath therapy has induced a significant ( $p < 0.01$ ) improvement of overall quality of life with reduction of pain at rest ( $2.1 \pm 1.5 \rightarrow 1.2 \pm 1.3$ ) and during daily activities ( $2.3 \pm 1.3 \rightarrow 1.4 \pm 1.3$ ). This has facilitated the physical function and psychosocial disability as shown by the questionnaires SF-36, WOMAC and SDS Zung. **Conclusions.** In conclusion our data suggest that mud-bath therapy with sulphurous mineral water can be considered as an important phase of the therapeutic strategy in OA.

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PMID: 22487501 [PubMed - in process]

## Paper 49

Clin Ter. 2011;162(2):e51-7.

### **[Knee osteoarthritis and SPA therapy: assessment of joint function and quality of life].**

[Article in Italian]

Costantino M, Filippelli A.

#### **Source**

Associazione F.I.R.S.Thermae, Divisione Idrologia Medica, Terme di Telese, Benevento, Italy. segreteria@firstthermae.org

#### **Abstract**

##### **OBJECTIVES:**

In industrialized countries the increase in life expectancy of the population has led to an increase in chronic diseases such as osteoarthritis (OA). Knee osteoarthritis for the high disability and psychological stress, not considered adequately, has negative impact on the quality of life. In this pathology SPA therapy, in particular the sulphur mud-bath therapy, can provide a stage of the therapeutic strategy. However, studies on the impact of SPA therapy on the quality of life in knee osteoarthritis are insufficient. The aim research was to evaluate the effectiveness of SPA therapy on chronic pain, joint function and psychological distress that characterize knee osteoarthritis.

##### **PATIENTS AND METHODS:**

The study has been performed on 44 subjects affected by knee Osteoarthritis, being 27 (61%) women and 17 (39%) men (mean age: 58±8.7 years, age range: 42-76 years). The investigated subjects were treated with a cycle of a combination of daily locally applied mud-packs and bicarbonate-sulphurous mineral bath water from Terme of Telese SpA (Benevento-Italy). At the beginning and at the end of the Spa therapy was evaluated the level of pain (using VAS scale), the degree of knee flexion (using goniometer), the level of anxiety and depression (using SDS Zung Test and SAS Zung test) and the impact of sulphurous mud-bath treatment on quality of life (using the algofunctional Lequesne indice).

##### **RESULTS:**

At the end of Spa therapy the results of our study have shown a significant ( $p<0.05$ ) reduction of the pain ( $1.8\pm1.6 \rightarrow 0,9\pm1,3$ ) and a significant ( $p<0.01$ ) increase of the knee flexion ( $79^{\circ}\pm22 \rightarrow 91.3^{\circ}\pm19$ ) with an improved quality of life.

##### **CONCLUSIONS:**

The data from this investigation seem to indicate that the SPA therapy may be useful in improving joint function and quality of life in knee osteoarthritis.

PMID: 21533309 [PubMed - indexed for MEDLINE]



## **Paper 50**

Clin Ter. 2006 Nov-Dec;157(6):525-9.

### **[Sulphur mud-bath treatment in osteoarthritis: therapeutic activity and efficiency on the quality of life].**

[Article in Italian]

Costantino M.

#### **Source**

Dip. Medicina Sperimentale sezione Farmacologia "L. Donatelli", Scuola di Specializzazione in Idrologia Medica, Centro Ricerche e Studi Termali srl-inserito in Anagrafe Nazionale di Ricerche del MIUR, Napoli, Italia. maria.costantino@unina2.it

#### **Abstract**

##### **OBJECTIVES:**

Osteoarthritis (OA) is a degenerative condition of the joints, involving: cartilage, synovia and bone. The onset is gradual with articular pain, functional difficulties, articular rigidity being accompanied by depression. Spa therapy with mud-bath treatment (FBT) is a promising management practice that can improve the quality of life for these patients. Few studies have investigated the impact of the FBT on the quality of life for patients with OA. The aim of our study was to investigate the "short-term" therapeutic effects and the impact on the quality of life using sulphur FBT in OA.

##### **PATIENTS AND METHODS:**

The study has been performed on 51 subjects affected by OA, being 32 (63%) women and 19 (37%) males (mean age: 62 +/- 1,2 years, age range: 44-77 years). The investigated subjects underwent 12 consecutive days sulphur mud-bath treatment (FBT) from Terme of Telesse in Telesse Terme (Benevento-Italy). At the beginning and at the end of the Spa therapy the clinical symptoms induced by OA and the impact of sulphur FBT treatment on quality of life were measured using VAS scale, WOMAC and SF-36 questionnaires.

##### **RESULTS:**

At the end of Spa therapy the results of our study, showed a significant ( $P < 0.05$ ) reduction of the symptoms and improved quality of life.

##### **CONCLUSIONS:**

The data of this first series of investigations suggests that sulphur FBT is useful in improving the quality of life of patients with OA.

PMID: 17256202 [PubMed - indexed for MEDLINE]

## **Paper 51**

Am J Phys Med Rehabil. 2010 Feb;89(2):125-32.

### **Short- and long-term effects of spa therapy in knee osteoarthritis.**

Fioravanti A, Iacoponi F, Bellisai B, Cantarini L, Galeazzi M.

#### **Source**

Rheumatology Unit, Department of Clinical Medicine and Immunological Sciences, University of Siena, Siena, Italy.

### **Abstract**

#### **OBJECTIVE:**

To assess both the short- and long-term effectiveness of spa therapy in patients with primary knee osteoarthritis in a prospective, randomized, single-blinded, controlled trial.

#### **DESIGN:**

Eighty outpatients were enrolled in this study; 40 patients were treated with a combination of daily local mud packs and bicarbonate-sulfate mineral bath water from the spa center of Rapolano Terme (Siena, Italy) for 2 wks, and 40 patients continued regular, routine ambulatory care. Patients were assessed at baseline time; after 2 wks; after 3, 6, and 9 mos after the beginning of the study and were evaluated by Visual Analog Scale for spontaneous pain, Lequesne index, Western Ontario and McMaster Universities Index for gonarthrosis, Arthritis Impact Measurement Scale-1, and symptomatic drug consumption.

#### **RESULTS:**

We observed a significant improvement of all evaluated parameters at the end of the cycle of spa therapy, which persisted throughout the whole of the follow-up period, whereas in the control group no significant differences were noted. This symptomatic effect was confirmed by the significant reduction of symptomatic drug consumption. Tolerability of spa therapy seemed to be good, with light and transitory side effects.

#### **CONCLUSIONS:**

The results from our study confirm that the beneficial effects of spa therapy in patients with knee osteoarthritis lasts over time, with positive effects on the painful symptomatology and a significant improvement on functional capacities. Spa therapy can represent a useful backup to pharmacologic treatment of knee osteoarthritis or a valid alternative for patients who do not tolerate pharmacologic treatments.

PMID: 19884812 [PubMed - indexed for MEDLINE]

### **Paper 52**

Clin J Pain. 2002 Sep-Oct;18(5):302-9.

#### **Contribution of individual spa therapies in the treatment of chronic pain.**

Strauss-Blasche G, Ekmekcioglu C, Vacariu G, Melchart H, Fialka-Moser V, Marktl W.

#### **Source**

Department of Physiology, University of Vienna, Austria. gerhard.strauss-blasche@univie.ac.at

### **Abstract**

#### **OBJECTIVES:**

The aim of the present study was to evaluate the contribution of individual spa therapies administered during a period of 3 weeks on measures of well being and pain in a sample of patients with chronic back pain.

### **DESIGN:**

One hundred fifty-three patients with chronic back pain undergoing inpatient spa therapy in Bad Tatzmannsdorf, Austria, participated in the study. According to the prescription of their spa physician, patients underwent two or more of the following treatments: mud packs, carbon dioxide baths, massages, exercise therapies, spinal traction, and electrotherapy. The outcome measures were general pain, back pain, negative mood, and health satisfaction. Regression analyses were conducted to predict the 4 outcome measures at the end of spa therapy and at 6 weeks' follow-up for all therapies applied. The pretreatment outcome measure, age, and sex were controlled for by entering them into the analysis.

### **RESULTS:**

Patients showed significant improvements in all 4 outcome measures. The prediction of improvement was generally small: only 1% to 11% of the change of the outcome measures could be explained by the type and number of therapies received. On a short-term basis, mud packs and exercise were found to be associated with a greater improvement in mood, whereas a greater frequency of massage therapy and carbon dioxide baths was associated with a smaller improvement in health satisfaction. On a long-term basis, exercise therapy and spinal traction were associated with a greater reduction in back pain.

### **CONCLUSIONS:**

The results indicate that, in addition to the individual therapies, other factors relating to spa therapy as a whole must contribute to overall treatment outcome. In addition, the results support the efficacy of exercise therapy for chronic back pain.

PMID: 12218501 [PubMed - indexed for MEDLINE]

## **Paper 53**

Joint Bone Spine. 2000;67(4):296-304.

### **Magnitude and duration of the effects of two spa therapy courses on knee and hip osteoarthritis: an open prospective study in 51 consecutive patients.**

Forestier R.

#### **Abstract**

#### **OBJECTIVE:**

To evaluate the effects of spa therapy on knee and hip osteoarthritis by studying patients given the same treatment on two different occasions.

#### **PATIENTS AND METHODS:**

A prospective study of two medically-supervised, 3-week spa therapy courses performed at an interval of about 1 year in 51 consecutive patients with knee and/or hip osteoarthritis, most of whom were overweight (mean body mass index, 30 +/- 5 kg/m<sup>2</sup>). Mean age was 66 years. Study data were collected over a 17-month period.

## **RESULTS:**

Lequesne's algofunctional index was significantly improved 5 and 8 months after the first course (by 1.74 +/- 2.2, P < 0.0001; and by 0.89 +/- 2.4, P = 0.017; respectively) and 5 months after the second course (by 1.26 +/- 3, P = 0.008). Walking distance showed comparable improvements. The decrease in medication use was not significant. No significant differences were found between the effects of the two courses after 20 days and 5 months. The advantages and drawbacks of the repeated treatment design used in this study are discussed.

## **CONCLUSION:**

Although some sources of bias could not be eliminated, our data suggest that spa therapy may be effective in knee and hip osteoarthritis. The repeated treatment design may prove useful for evaluating treatments to which patients cannot be blinded.

## **Comment in**

Evaluation of spa therapy in rheumatology. [Joint Bone Spine. 2000]

PMID: 10963077 [PubMed - indexed for MEDLINE]

## **Paper 54**

Isr Med Assoc J. 2008 May;10(5):365-9.

## **Balneotherapy in elderly patients: effect on pain from degenerative knee and spine conditions and on quality of life.**

Gaál J, Varga J, Szekanez Z, Kurkó J, Ficzer A, Bodolay E, Bender T.

## **Source**

Department of Rheumatology, Kenézy Gyula County Hospital, Debrecen, Hungary. gaalja@freemail.hu

## **Abstract**

### **BACKGROUND:**

Balneotherapy is an established treatment modality for musculoskeletal disease, but few studies have examined the efficacy of spa therapy in elderly patients with degenerative spine and joint diseases.

### **OBJECTIVES:**

To assess the effects of balneotherapy on chronic musculoskeletal pain, functional capacity, and quality of life in elderly patients with osteoarthritis of the knee or with chronic low back pain.

### **METHODS:**

The 81 patients in the study group underwent a 1 day course of 30 minute daily baths in mineral water. Changes were evaluated in the following parameters: pain intensity, functional capacity, quality of life, use of non-steroidal anti-inflammatory or analgesic drugs, subjective disease severity perceived by the patients, investigator-rated disease severity, and severity of pain perceived by

the patients. We analyzed the results of 76 subjects as 5 did not complete the study.

### **RESULTS:**

Compared to baseline, all monitored parameters were significantly improved by balneotherapy in both investigated groups. Moreover, the favorable effect was prolonged for 3 months after treatment.

### **CONCLUSIONS:**

This study showed that balneotherapy is an effective treatment modality in elderly patients with osteoarthritis of the knee or with chronic low back pain, and its benefits last for at least 3 months after treatment.

PMID: 18605361 [PubMed - indexed for MEDLINE] **Free full text**

### **Paper 55**

Clin Ter. 2003 Jan-Feb;154(1):45-8.

### **[Fangothrapy in chronic degenerative rheumatic diseases].**

[Article in Italian]

Grassi M, Lucchetta MC, Rini GB, Raffa S.

### **Source**

Dipartimento di Clinica e Terapia Medica applicata, Università di Roma La Sapienza, Italia. marcellograssi@hotmail.com

### **Abstract**

The authors remind the historical role of the mud-therapy in the care of chronic degenerative rheumoarthropaties, namely osteoarthritis. The main researches belong activity of muds on plasmatic hormones, cytokines, endorphins; a great deal of care is devoted to evaluation of efficacy of mud therapy and relating end points. The clinic outcomes of mud therapy, namely in osteoarthritis patients, were referred. Altogether the studies stress the employ of mud therapy in the treatment of osteoarthritis, the consequences of traumas, some dismetabolic chronic arthropaties, and fibromyalgic syndromes.

PMID: 12854283 [PubMed - indexed for MEDLINE]

### **Paper 56**

J Clin Rheumatol. 2002 Aug;8(4):197-203.

### **Therapy with mud compresses for knee osteoarthritis: comparison of natural mud preparations with mineral-depleted mud.**

Flusser D, Abu-Shakra M, Friger M, Codish S, Sukenik S.

### **Source**

Rheumatic Diseases Unit, Internal Medicine "D" Department, Soroka University Medical Center and the Faculty of Health Sciences, Ben Gurion University of the Negev, Beer-Sheva, Israel.

### **Abstract**

Mud pack therapy is an alternative mode of treatment for rheumatic diseases. It is based on the application of heated mud packs to the entire body or to specific areas, such as over joints. The aim of the current study was to evaluate the efficacy of treatment with mud compresses at patients' homes for osteoarthritis of the knee. Fifty-eight patients with osteoarthritis of the knee were enrolled in a prospective, double-blinded, controlled study. Forty patients were treated with natural mineral-rich mud compresses and 18 patients were treated with mineral-depleted mud compresses. Mud compresses were applied 5 times each week during 3 weeks for a total of 15 treatments. Patients were assessed at baseline, at completion of the 3-week treatment period, and twice after the conclusion of the treatment period—after 1 month and after 3 months. The main outcome measures were the Lequesne Index of severity of knee osteoarthritis, patient self-assessment of pain, and severity of knee pain on a visual analog scale. A reduction of 20% or more in the pain scores was considered clinically significant. In the group treated with natural mud compresses, a significant reduction in knee pain was observed at all assessments. Similarly, improvement in the Lequesne Index was seen at the end of therapy and a month after treatment. In the control group, given mineral-depleted mud compresses, no significant change in knee pain was seen at any assessment. Improvement in the Lequesne Index was seen 1 and 3 months after completion of the therapy, but not at the end of therapy. Seventy-two percent of the patients in the treatment group had an improvement of >20% in self-assessment of knee pain, compared with 33% in the control group ( $p = 0.005$ ). The data suggest that treatment with mud compresses, but only in their natural form, temporarily relieves pain in patients with osteoarthritis of the knees. We believe that treatment with mud compresses might augment conventional medical therapy in these patients.

## Comment in

It's a dirty job but someone has to do it: thoughts about mud and other complementary and alternative therapies. [J Clin Rheumatol. 2002]

PMID: 17041359 [PubMed]

## Paper 57

J Altern Complement Med. 2008 Jun;14(5):559-65.

### **Does mud pack treatment have any chemical effect? A randomized controlled clinical study.**

Odabasi E, Turan M, Erdem H, Tekbas F.

#### **Source**

Department of Medical Ecology and Hydroclimatology, Gulhane School of Medicine, Ankara, Turkey. ersinodabasi@hotmail.com

#### **Abstract**

##### **OBJECTIVE:**

The aim of this study was to reveal the efficacy of mud pack treatment in patients with knee osteoarthritis and to find the contribution of chemical factors to the build up of these effects.

##### **METHODS:**

Sixty patients were randomly assigned to directly applied mud pack (study) group or to nylon-covered mud pack (control) group. Thirty patients in the study

group had mud application 15 times to both knees: heated mud, up to 43 degrees C, was applied to skin directly for 30 minutes. Thirty patients in the control group had the same treatment as the study group except heated mud was applied over an impermeable nylon pack. Primary outcome measures of the study were the Western Ontario and McMaster Universities (WOMAC) index, pain intensity on a visual analog scale (VAS), patient's assessment of disease severity index, physician's assessment of disease severity index, and analgesic consumption. The patients were evaluated before and after (end of 15th application) the intervention and followed up for 24 weeks at 4-week intervals. The results were assessed on an intent-to-treat basis.

## **RESULTS:**

As compared to the baseline, significant decreases were observed in WOMAC, pain intensity, disease severity index scores, and analgesic consumption in both groups after the intervention. Observed improvements in the study group were found to be superior to the control during the whole postintervention follow-up, except for analgesic consumption in the third week. A significant number of patients in the study group showed minimal clinically important improvement as compared to the control group.

## **CONCLUSION:**

Mud pack treatment significantly improved the pain and functional status of patients with knee osteoarthritis, whether applied directly or coated with nylon. Direct application was found to be superior, which implies chemical properties of the mud contribute to the build up of therapeutic effect.

PMID: 18564957 [PubMed - indexed for MEDLINE]

## **Paper 58**

Minerva Med. 2000 Oct;91(10):239-45.

## **[Beta-endorphin and stress hormones in patients affected by osteoarthritis undergoing thermal mud therapy].**

[Article in Italian]

Pizzoferrato A, Garzia I, Cenni E, Pratelli L, Tarabusi C.

## **Source**

Laboratorio di Patologia Clinica Istituti Ortopedici Rizzoli, Bologna.

## **Abstract**

### **BACKGROUND:**

Thermal mud is a therapeutic agent widely used in the treatment of painful arthritic processes. The mechanism by which mud therapy works is still not well known. Its effect continues for months after completion of treatment. In order to verify whether thermal mud treatment brings about changes in the production of hormone peptides from proopiomelanocortin, the levels of plasma beta-endorphin and some hormones of the pituitary-adrenal glands (ACTH and cortisol) were determined in patients affected by osteoarthritis undergoing thermal mud therapy.

### **METHODS:**

The levels of plasma beta-endorphin and some hormones of the pituitary-adrenal glands (ACTH and cortisol) were assessed by radiometric methods in

seventeen males affected by osteoarthritis. The patients underwent a cycle of twelve sessions of thermal mud therapy. The tests were carried out immediately before thermal treatment, immediately after the first session, twelve days after the start of treatment, and again one month after completion of the treatment.

### **RESULTS:**

beta-endorphin levels decreased significantly twelve days after the start of treatment. The level was still lower, although not significantly, even thirty days after completion of the treatment. Plasma ACTH also decreased during treatment. The decrease of this hormone was progressive and persisted after completion of treatment. Significant variations compared to baseline were found only thirty days after completion of treatment. Plasma cortisol decreased significantly after only one session of mud therapy. This hormone did not decrease any further during treatment, however, after twelve days it was still significantly lower than baseline. After completion of treatment, cortisol slightly increased, but thirty days later it was still lower, although not significantly, than baseline.

### **CONCLUSIONS:**

It may be suggested that thermal treatment, by reducing inflammation, reduced pain and therefore diminished the cause of stress.

PMID: 11236389 [PubMed - indexed for MEDLINE]

### **Paper 59**

Int J Clin Pharmacol Res. 2000;20(3-4):69-80.

### **Mud bath therapy influences nitric oxide, myeloperoxidase and glutathione peroxidase serum levels in arthritic patients.**

Bellometti S, Poletto M, Gregotti C, Richelmi P, Bertè F.

#### **Source**

P. d'Abano Scientific Research Centre, Via P. d'Abano 11, 35031 Abano T., PD, Italy. [terme@studitermali.org](mailto:terme@studitermali.org)

#### **Abstract**

Nitric oxide (NO) has recently been proposed as an important mediator in inflammatory phases and in loss of cartilage. In inflammatory arthritis NO levels are correlated with disease activity and articular cartilage is able to produce large amounts of NO with the appropriate inducing factors such as cytokines and/or endotoxin. Neutrophils also play an important role in inflammatory reactions and the level of myeloperoxidase, a constituent of neutrophil granules, is related to the intensity of the inflammation. Because there is evidence that suggests that mud packs influence the main cytokines involved in cartilage damage, we tried to determine whether NO and myeloperoxidase are involved in the mechanisms of action of mud bath treatment. We enrolled 37 subjects and randomly assigned them to two groups: 19 patients underwent mud bath treatment (group A) while 18 patients underwent bath treatment alone. Blood samples were obtained before and after the treatment cycles to assay serum levels of NO, myeloperoxidase (MPO) and glutathione (GSH)-peroxidase. The results showed a statistically significant decrease in NO and myeloperoxidase serum values in groups A and B, while GSH-peroxidase was not significantly increase in either of the groups; no correlation was found between NO, myeloperoxidase and GSH-peroxidase serum values. Mud bath treatment can exert beneficial effects on cartilage homeostasis and inflammatory reactions,



influencing NO and decreasing myeloperoxidase serum values. The increase in GSH-peroxidase was not correlated with the reduction of other biochemical markers, suggesting that mud bath treatment has different mechanisms of action.

PMID: 11314241 [PubMed - indexed for MEDLINE]

## **Paper 60**

Int J Clin Pharmacol Res. 2005;25(2):77-94.

### **Production of matrix metalloproteinases and their inhibitors in osteoarthritic patients undergoing mud bath therapy.**

Bellometti S, Richelmi P, Tassoni T, Bertè F.

#### **Source**

Postgraduate School of Medical Hydrology, Department of Internal Medicine, Faculty of Medicine, University of Pavia, Italy. [simonab@studitermali.org](mailto:simonab@studitermali.org)

#### **Abstract**

Several studies have demonstrated that matrix metalloproteinases (MMPs) are frequently implicated in the destruction of articular cartilage in arthritis. The control of MMP activity is dependent on the local concentration of tissue inhibitors of metalloproteinases (TIMPs), and the imbalance of the enzyme-to-inhibitor ratios plays an important role in the remodeling of articular tissues. Some cytokines such as interleukin (IL)-1 and tumor necrosis factor (TNF)-alpha which regulate leukocyte activities, promote MMP secretion and, as a consequence, cartilage degradation. The aim of the present study was to investigate whether a natural treatment is effective in reducing cartilage inflammation and degradation by influencing MMP and TIMP serum levels. Eighty patients with osteoarthritis (OA) were enrolled in the trial and were divided into group A (30 patients who did not undergo mud bath therapy), group B (28 patients repeating mud bath therapy more than 5 times and less than 10) and group C (22 patients repeating mud bath therapy more than 10 times). Blood samples were obtained from all the patients for assay of MMP-1, -2, -3, -8 and -9 and TIMP-1 and -2. The parameters were determined by an ELISA technique. Statistical indexes were calculated for each parameter and mean values were compared. The differences between mean values of MMP-3, -8 and -9 were statistically significant between group A and the treated groups (B and C). Analysis of variance established a significant difference ( $p < 0.05$ ) between groups A and C in mean serum levels of MMP-8, MMP-9 showed a statistically significant difference ( $p < 0.05$ ) in mean serum concentration between groups A and B. Regression analysis showed a very high  $R^2$  between MMP-2 and TIMP-2. One of the most interesting findings in this study was that MMP-3 serum levels were significantly lower in the treated groups, since this enzyme plays an important role in cartilage degradation, suggesting that mud bath therapy contributes to matrix integrity in OA cartilage. In contrast, MMP-8 and -9 were higher in the treated subjects and no correlation with TIMPs was evident. One possible explanation is that these enzymes are required for the efficient degradation and removal of already compromised cartilage matrix and that they operate as part of a matrix turnover and repair process. In conclusion, our data suggest that mud bath therapy alone is not able to influence chondrocyte metabolic activity in the advanced phases of OA. There could be a synergic and sequential association with pharmacologic therapy and/or interventions.

PMID: 16060398 [PubMed - indexed for MEDLINE]

## Paper 61

Int J Tissue React. 2002;24(2):57-64.

### **Both serum receptors of tumor necrosis factor are influenced by mud pack treatment in osteoarthrotic patients.**

Bellometti S, Galzigna L, Richelmi P, Gregotti C, Bertè F.

#### **Source**

Pietro d'Abano Research Centre, Padova, Italy. simonab@intercity.it

#### **Abstract**

Several authors have demonstrated the pivotal role of proinflammatory cytokines in inducing progressive cartilage degradation and secondary inflammation of the synovial membrane in osteoarthritis (OA). It has recently been established that tumor necrosis factor (TNF)-alpha plays a well-defined role in the pathophysiology of inflammatory joint diseases and that binding to circulating soluble TNF-alpha receptors can inactivate it. We investigated the influence of mud pack treatment, which is able to diminish TNF-alpha serum values, on specific TNF receptor (sTNF-R) levels. Thirty-six patients with OA were enrolled and randomized into two groups. Group A underwent mud pack treatment and group B underwent thermal bath treatment. A group of 20 healthy untreated subjects was used as a control. Blood samples were collected at baseline and after treatment, and assays of sTNF-R55 and sTNF-R75 were performed in both groups. We found small changes in sTNF-Rs serum values but these were not statistically significant. sTNF-R55 serum values decreased by 0.4% after the therapy in group A, while in group B the decrease was -17.7%. sTNF-R75 was reduced by -21.17% in group A and by -10.6% in group B. In conclusion, through its thermic and ant/inflammatory activity mud pack treatment shows complex interaction with the most common factors of inflammatory and cartilage degradation. Our results suggest that the thermic component of this natural treatment is mainly involved in modulating inflammatory reaction and cartilage damage through binding of the circulating TNF, which controls the activation of the cells responsible for the production of proinflammatory cytokines.

PMID: 12182234 [PubMed - indexed for MEDLINE]

## Paper 62

Joint Bone Spine. 2007 Oct;74(5):436-9. Epub 2007 May 30.

### **Mud-bath treatment in spondylitis associated with inflammatory bowel disease--a pilot randomised clinical trial.**

Cozzi F, Podswiadek M, Cardinale G, Oliviero F, Dani L, Sfriso P, Punzi L.

#### **Source**

Division of Rheumatology, Department of Clinical and Experimental Medicine, University of Padova, Via Giustiniani 2, 35128 Padova, Italy. franco.cozzi@unipd.it

#### **Abstract**

##### **OBJECTIVES:**

The objective of this study was to evaluate the effects and the tolerability of mud packs and thermal baths in a group of patients affected with this disease.

## **METHODS:**

Twenty-four patients with spondylitis and Crohn's disease or ulcerative colitis, treated with 5-ASA or sulfasalazine, were randomised and assessed by an investigator independent from the spa staff: 12 were submitted to a cycle of mud-bath treatment (12 mud packs and 12 thermal baths over a period of two weeks) and 12 were enrolled as controls. Patients were evaluated by BASDAI, BASFI, BAS-G and VAS for back pain before, at the end of a cycle of mud-bath treatment, and after 12 and 24 weeks. C reactive protein serum levels detected by high sensitivity nephelometric method and gut symptoms evaluated by CDAI or Powell-Tuck index were assessed at the same time periods.

## **RESULTS:**

A significant reduction of clinical evaluation indices of spondylitis was observed at the end of the cycle of mud-bath treatment. BASDAI50 improvement remained significant until the end of the follow-up (24 weeks). C reactive protein serum levels didn't show significant changes. No patient referred any gut symptom exacerbation. No significant changes in clinical evaluation indices, in IBD activity indices and in CRP serum levels were observed in the control group.

## **CONCLUSION:**

Mud-bath treatment in patients with spondylitis associated with inflammatory bowel disease is well tolerated and may improve spinal symptoms and function for several months.

PMID: 17590368 [PubMed - indexed for MEDLINE]

## **Paper 63**

Joint Bone Spine. 2001 Dec;68(6):499-503.

## **Effect on osteoarthritis of spa therapy at Bourbonne-les-Bains.**

Guillemin F, Virion JM, Escudier P, De Talancé N, Weryha G.

## **Source**

Epidemiology and Clinical Evaluation Department, UPRES EA 1124, CHU de Nancy, Hôpital Marin, Nancy, France. eval@chu-nancy.fr

## **Abstract**

### **OBJECTIVES:**

Several studies suggest a beneficial overall effect of spa therapy in chronic musculoskeletal diseases. The present open controlled study investigated the effects of spa therapy at Bourbonne-Les-Bains, France, in patients with hip or knee osteoarthritis or low back pain. PATIENTS and

### **METHODS:**

In 1998, 102 men and women older than 50 years were included in the study. All had low back pain or lower limb osteoarthritis, and none had contraindications to spa therapy. Quality of life was assessed three times at intervals of 4 weeks, twice before and once immediately after 3 weeks of spa therapy, using the Duke Health Profile (five dimensions and five dysfunctions).

### **RESULTS:**

Mean age was 66.4 years, and 67% of the patients were women. Quality of life was markedly decreased as compared to the population at large (1996, CFES). The two pretreatment evaluations produced similar quality-of-life scores. Spa therapy was associated with significant improvements in overall quality of life (P=0.004), self-esteem (P=0.009), and pain (P=0.01).

### **CONCLUSION:**

These findings support those of other studies conducted in France and in other European countries. They indicate that patients report meaningful improvements in their quality of life after spa therapy.

PMID: 11808987 [PubMed - indexed for MEDLINE]

### **Paper 64**

Acta Orthop Traumatol Turc. 2010;44(1):42-7.

### **Comparison of intra-articular hyaluronic acid injections and mud-pack therapy in the treatment of knee osteoarthritis.**

Bostan B, Sen U, Güneş T, Sahin SA, Sen C, Erdem M, Erkorkmaz U.

### **Source**

Department of Orthopedics, Gaziosmanpaşa University, Tokat, Turkey.  
borabostan@gmail.com

### **Abstract**

#### **OBJECTIVES:**

Conservative treatment should be tried prior to surgical treatment in knee osteoarthritis. This study was designed to evaluate the short-term effects of mud-pack therapy on pain relief and functional improvement in knee osteoarthritis in comparison with intra-articular hyaluronic acid injections.

#### **METHODS:**

The study included 23 patients who were diagnosed as having knee osteoarthritis according to the ACR (American College of Rheumatology) criteria, and had complaints lasting for more than three months. All the patients had stage 2 or 3 osteoarthritis radiographically according to the Kellgren-Lawrence criteria. Twelve patients (3 males, 9 females; mean age 54+/-6 years; range 46 to 67 years) received mud therapy bilaterally. Mud packs were heated to 45 degrees C and applied on both knees for 30 minutes daily for a total of 12 weekdays. Eleven patients (2 males, 9 females; mean age 53+/-9 years; range 40 to 66 years) received a total of three bilateral intra-articular hyaluronic acid injections, each interspersed by weekly intervals. The patients were evaluated before and after treatment in terms of pain and functionality using the pain subscale of the WOMAC (Western Ontario and McMaster Universities) osteoarthritis index, Hospital for Special Surgery (HSS) score, and Knee Society clinical rating system (knee and function scores). The patients were followed-up for a mean of 5.9+/-6.3 months (range 4 to 8 months) after mud-pack therapy, and 5.8+/-0.8 months (range 5 to 7 months) after intra-articular hyaluronic acid injections.

#### **RESULTS:**

No significant differences were found between the two groups with respect to pre-and posttreatment WOMAC, HSS, and knee and function scores (p>0.05). The scores of all instruments showed significant improvements following

treatment in both groups ( $p < 0.001$ ). Posttreatment changes in relation to baseline scores did not differ significantly between the two groups ( $p > 0.05$ ).

### **CONCLUSION:**

Treatment of knee osteoarthritis with intra-articular hyaluronic acid injections or mud-pack therapy yielded similar results in the short-term in terms of functional improvement and pain relief. Mud-pack therapy is a noninvasive, complication-free, and cost-effective alternative modality for the conservative treatment of knee osteoarthritis.

PMID: 20513990 [PubMed - indexed for MEDLINE] **Free full text**

### **Paper 65**

Med Care. 1998 Sep;36(9):1309-14.

### **Use of spa therapy to improve the quality of life of chronic low back pain patients.**

Constant F, Guillemin F, Collin JF, Boulangé M.

#### **Source**

School of Public Health, Institute of Hydrology, University Henri Poincaré, Faculty of Medicine, Nancy, France.

#### **Abstract**

##### **OBJECTIVES:**

This study assessed the effectiveness of adding spa therapy to usual drug treatment in chronic low back pain patients.

##### **METHODS:**

A total of 224 patients were assigned randomly to either a treatment ( $n=128$ ) or a control ( $n=96$ ) group. Subjects in both groups received usual drug therapy. Those in the treatment group also underwent spa therapy in Vittel, France, for 6 days a week for 3 consecutive weeks. Effectiveness was assessed using a quality-of-life scale (the Duke Health Profile), clinical measures, and the Roland and Morris disability questionnaire. Groups were compared using an analysis of variance with repeated measures.

##### **RESULTS:**

At both 3 weeks and 3 months, patients in the treatment group exhibited significant improvement in measures of: physical and mental dimensions of quality of life, anxiety, depression, pain duration, pain intensity, and functional disability.

##### **CONCLUSION:**

This study suggests that spa therapy is an effective treatment for chronic low back pain patients.

#### **Comment in**

[Spa therapy: panacea or placebo? \[Med Care. 1998\]](#)

PMID: 9749654 [PubMed - indexed for MEDLINE]

## Paper 66

Br J Rheumatol. 1997 Jan;36(1):77-81.

### **Prolonged effects of 3 week therapy in a spa resort on lumbar spine, knee and hip osteoarthritis: follow-up after 6 months. A randomized controlled trial.**

Nguyen M, Revel M, Dougados M.

#### **Source**

René Descartes University, Paris, France.

#### **Abstract**

Spa therapy is frequently used in daily rheumatological practice, but its benefit remains to be evaluated. A prospective randomized controlled study was conducted in 1993 in patients with osteoarthritis of the hip, knee or lumbar spine. Treatment was either spa therapy at Vichy (France) of 3 weeks duration (spa group) or usual therapy (control group). Assessment criteria were pain (visual analogue scale), functional impairment (Lequesne's index for hip or knee disease, Main and Waddell's for lumbar spinal diseases), quality of life index [revised Arthritis Impact Measurement Scale (AIMS2)], and analgesic and/or non-steroidal anti-inflammatory drug (NSAID) consumption. Patients were included by randomization into one of the two arms (spa or control) and assessment criteria were collected before spa therapy or the control period, and 3 and 24 weeks thereafter. A total of 188 patients (lumbar spine 95, knee 64, hip 29) were included in the study (spa group 91, control group 97). Changes in the assessment criteria after a 6 month follow-up period showed improvement in terms of pain, functional impairment and quality of life, with a reduced intake of symptomatic drugs (NSAID and analgesic drugs) in the spa group. This study suggests that spa therapy of 3 weeks duration has a prolonged, beneficial, symptomatic effect in osteoarthritis.

PMID: 9117181 [PubMed - indexed for MEDLINE] [Free full text](#)

## Paper 67

Int J Clin Pharmacol Res. 1997;17(4):149-53.

### **Cytokine levels in osteoarthrosis patients undergoing mud bath therapy.**

Bellometti S, Giannini S, Sartori L, Crepaldi G.

#### **Source**

Centro Studi Termali Pietro D'Abano, Abano Terme, Italy.

#### **Abstract**

Osteoarthritis is an important rheumatic condition characterized by the progressive destruction of cartilage. The pathophysiologic phenomena leading to the pathologic changes in the joint appear to result from biomechanical factors and activation of final common pathways of tissue damage influencing chondrocyte homeostasis and a functional program. Several cytokines and growth factors are reported to be responsible for inflammation and cartilage degradation. Among these, IL-1 and TNF alpha have been suggested as important in promoting cartilage inflammation and tissue destruction, while IGF I has a protective influence on cartilage structure. Chondrocytes and their metabolism have gained interest as targets of drug intervention; the results of

this study confirm that mud bath therapy is also able to influence chondrocyte activities. Our data suggest that mud bath therapy influences cytokines related to osteoarthritis pathomechanism and maintenance, and encourage further investigations to evaluate possible synergism between pharmacological treatment and mud bath therapy.

PMID: 9526176 [PubMed - indexed for MEDLINE]

# Annex D

## RESPIRATORY SYSTEM

### Paper 1

[Acta Otolaryngol.](#) 2007 Jun;127(6):613-7.

**Sulphurous-arsenical-ferruginous (thermal) water inhalations reduce nasal respiratory resistance and improve mucociliary clearance in patients with chronic sinonasal disease: preliminary outcomes.**

[Staffieri A](#), [Abramo A](#).

### Source

Department of Medical and Surgical Specialties, Section of Otolaryngology, University of Padova, Padova, Italy. [alberto.staffieri@unipd.it](mailto:alberto.staffieri@unipd.it)

### Abstract

#### CONCLUSIONS:

In order to confirm these preliminary results, a prospective double-blind study has been instituted in Padova University ENT Section to compare the efficacy of sulphurous-arsenical-ferruginous thermal water nasal irrigations vs isotonic sodium chloride solution nasal irrigations after functional endoscopic sinus surgery for chronic sinusitis.

#### OBJECTIVES:

Despite their widespread use, much uncertainty exists about the indications and therapeutic mechanisms of nasal thermal water inhalations in the treatment of sinonasal chronic disease. The aim of the present study was to evaluate the effects of sulphurous-arsenical-ferruginous thermal water inhalations on nasal respiratory flow, mucociliary transport, nasal cytology, and chemo-physics of nasal mucus in a group of consecutive patients with chronic sinonasal disease.

#### PATIENTS AND METHODS:

Thirty-seven patients with chronic sinonasal disease underwent a 12-day course of sulphurous-arsenical-ferruginous thermal water warm vapour inhalations (38 degrees C) followed by nasal aerosol of the same thermal water (7 microns micelle).

#### RESULTS:

This preliminary study showed that a course of sulphurous-arsenical-ferruginous thermal water inhalations determined a significant improvement in nasal flow and reduction of nasal resistance; a statistically significant reduction of mean mucociliary transport time, from pathologic to physiologic values, has also been shown. Statistical analysis of our data confirmed that the presence of nasal bacteria was significantly reduced by thermal water inhalations.



## Paper 2

[Ann Pediatr \(Paris\). 1992 May;39\(5\):293-9.](#)  
[Spa treatment in pediatric pneumo-allergology and ENT.](#)

[Article in French]

[Jean R, Fourot-Bauzon M, Perrin P.](#)

### Source

Hôpital Necker Enfants Malades, Médecin à Allevard-les-Bains.

### Abstract

Each year in France, 42,000 children receive spa therapy, which is covered by the national health care insurance system. In over three cases out of four, the treatment is ordered by the child's physician for respiratory tract disease which fails to respond adequately to conventional therapy. Asthma, recurrent bronchitis, and spasmodic cough are the main indications in pneumo-allergology; seromucous otitis media, naso-sinusitis and refractory pharyngitis are the most common pediatric ENT diseases treated in spa centers. The two main types of mineral water used are sulfur-rich waters in patients with prominent infection and chloride and bicarbonate-rich waters when allergy is the main problem. Experimental studies point to the fact that these waters have immunomodulating effects. However, other therapeutic interventions in spa centers, including rehabilitation and health education, also play a role. Evaluations of spa therapy for respiratory tract diseases carried out by government agencies have demonstrated decreases in school absenteeism and above all in the use of drugs in treated patients. The future of pediatric spa therapy will likely depend on the development of preventive interventions in spa centers.

PMID:

1616245

[PubMed - indexed for MEDLINE]

## Paper 3

[Ateneo Parmense Acta Biomed. 1976 Sep-Oct;42\(5\):635-42.](#)

[\[The curative action of Monticelli Terme's water in upper respiratory tract diseases \(author's transl\)\].](#)

[Article in Italian]

[Turchi R, Jemmi G, Barani B.](#)

### Abstract

The Authors study the action of the sodio bromide-iodic water of Monticelli Terme in upper respiratory tract disease and particularly assert that is not to neglect the organic ground on which establishes mucosa's disease. Therman treatment gives the best therapeutic results in every patient presenting chronic inflammatory processes of the upper respiratory trach alternating periods of quiescency and of activity, and poor therapeutic action in patients presenting chronic inveterate diseases with great alterations in vascular and glandular components of the mucosa.

PMID:

1021139  
[PubMed - indexed for MEDLINE]

#### **Paper 4**

**Recenti Prog Med. 2008 Jun;99(6):314-21.**

**Hydrological indications in the therapy of pharyngitis.**

[Article in Italian]

**Olina M, Aluffi Valletti P, Pia F, Toso A, Borello G, Policarpo M, Garavelli PL.**

#### **Source**

Clinica ORL, Università del Piemonte Orientale, Novara.

#### **Abstract**

Pharyngitis is an inflammatory disease of the mucosal and submucosal structures of the throat. Infection may or may not be a component of the disease. Pharyngitis is one of the common illness for which patients visit primary care physicians. Most of them are diagnosed by clinical evaluation and usually respond to treatment with antibiotics, but exceptions occur when pharyngitis is caused by non bacterial inflammatory processes like virus, mycoses, reflux of gastric juices, tobacco or alcohol abuse. In these cases, as alternative and preventive, could be indicated the thermal therapy. For many centuries thermal waters have been used in the treatment of chronic inflammations of the upper respiratory airway, such as pharyngitis, with good results. Different thermal waters are currently used, in particular sulfur or sulfur- salty- bromine-, iodine- or sulfur-sulfate-bicarbonate-carbonate alkaline or sulfur-arsenical-ferruginous, normally utilized by inhalation or irrigation or aerosol-therapy. The principal pharmacological activity of these waters is connected to the concentrations of H<sub>2</sub>S, halogens (Iodine e Bromine), sulfates, arsenic and the level of radioactivity, concerning their antimicrobial power and the mucolytic effect of sulphur.

PMID:

18710064

[PubMed - indexed for MEDLINE]

#### **Paper 5**

**Clin Ter. 2008 May-Jun;159(3):181-8.**

**[Clinical evaluation of the efficacy of Salsomaggiore (Italy) thermal water in the treatment of rhinosinusal pathologies].**

[Article in Italian]

**Passali D, Lauriello M, Passali GC, Passali FM, Cassano M, Cassano P, Bellussi L.**

#### **Source**

Università degli Studi di Siena Istituto di Discipline ORL, Italia.  
d.passali@virgilio.it

## **Abstract**

### **OBJECTIVES:**

Aim of the research was to demonstrate the efficacy of a treatment with thermal water as nasal spray (Salsomaggiore Italy) vs saline on chronic rhinosinusitis with/out nasal polyps.

### **MATERIALS AND METHODS:**

55 patients affected by chronic rhinosinusitis with/out I degree nasal polyposis randomised into two groups were enrolled. 30 patients of the study group were treated with thermal water nasal spray 4 times/day for 4 weeks. 25 patients of the control group were treated, with the same protocol, with saline. At the beginning and at the end of the study, in all the subjects the clinical history, objective examination and the instrumental analysis of nasal functions by active anterior rhinomanometry, mucociliary transport (MCT) time determination and nasal cytology were performed.

### **RESULTS:**

At the end of the treatment patients in the study group showed an improvement statistically significant, with respect to the control group, of headache, rhinorea and hiposmia. Significant differences were also observed between the study and control group concerning objective examination (nasal mucosa appearance and crusts) and instrumental analysis (rhinomanometric values and mucociliary transport times). Nasal cytology (epithelial and goblet cells, neutrophils, eosinophils, bacteria) improved in both groups without any statistical difference.

### **CONCLUSIONS:**

Thermal water (Salsomaggiore Italy) nasal spray showed a greater efficacy with respect to saline in the treatment of patients affected by chronic rhinosinusitis.

PMID:

18594749

[PubMed - indexed for MEDLINE]

## **Paper 6**

**Clin Ter. 2003 Nov-Dec;154(6):395-400.**

**[Inhalation therapy with sulphur water in ORL: clinical-experimental study].**

[Article in Italian]

**Costantino M, Rossi F, Lampa E.**

### **Source**

Seconda Università degli Studi di Napoli, Dipartimento di Medicina Sperimentale Sezione Farmacologia L. Donatelli, Scuola di Specializzazione in Idrologia Medica, Via Costantinopoli, 16, 80138 Napoli. mariacostantino@katamail.com

### **Abstract**

#### **OBJECTIVE:**

Several clinics and experimental researches have highlighted the utility of the inhalant mineral therapy in numerous diseases to load of the tall and low respiratory streets. Aim of the our clinical-experimental study has been that of appraise "to brief term" the curative effects and the adverse reactions of a thermal inhalant treatment with sulphur water in the care of diseases ORL apparatus (laryngitis, pharyngitis, rhinitis, rhinosynusitis), appraise the course of some End points to distance.

#### **PATIENT AND METHODS:**

The study has been channel on a champion of 83 subjects of which 45 of male sex and 38 of female sex with age serious equal average to 53 years +/- 2.6. The subjects of the examined champion that affections from diseases inflammatory chronic of ORL relevance (laryngitis, pharyngitis, rhinitis) were subjected to a cycle of sulphur mineral inhalant therapy disbursed with businesslike individual of inhalations to bud of vapor to the T of 38 degrees C to 20 cm from the face with duration of 10 min, follows from aerosol for likewise minutes. To the beginning and at the end of the sulphur mineral inhalant cycle has been valued the subjective symptomatology susceptible of amelioration, some End Points to distance and the adverse reactions.

#### **RESULTS:**

The data seem to highlight the end cycle curative sulphur mineral inhalant an significant ( $P < 0.05$ ) amelioration of best part of the symptoms examined like cough, nasal itch, expectoration [etc]. The analysis of the End Points to advised Distance show an significant ( $P < 0.05$ ) progressional diminution of such indicators to succession of the annual continuity of the inhalant sulphur mineral treatment.

#### **CONCLUSIONS:**

The results of such research seem to demonstrate that the inhalant sulphur mineral therapy can induced notable benefit in different inflammatory chronic diseases of ORL relevance in peculiar in the first ten of life with a positive relapse on some End Points to distance and an excellent local and systemic tolerable.

PMID:

14994519

[PubMed - indexed for MEDLINE]

### **Paper 7**

**Clin Ter. 1996 Dec;147(12):645-52.**

**[Crenotherapy in sports medicine: the state of the art].**

[Article in Italian]

**Grassi M, Lazzari S, Sottili S.**

#### **Source**

Istituto di Idrologia Medica, Università degli Studi di Roma La Sapienza.

#### **Abstract**

The existing relationship linking thermal and sport medicine has developed with time. This is shown by the established beneficial effects of thermal treatments (mineral waters, mud baths, balneotherapy, aerosol applications) in a wide range of sport and non-sport related injuries. The muscle fatigue syndrome is a condition particularly worrisome for sports practising individuals. This condition impairs the cardiovascular system, as well as hematologic, renal and gastrointestinal functions, acting via biochemical and metabolic modifications of the organism, which have effects also on the psyche of the subject. The treatment of this syndrome includes the use of specific mineral waters, which underscores that the correct hydration of the organisms is a precondition to achieve high performance levels. Traumas involving muscles and skeletal segments, and precocious arthrosis occur with higher frequency in sportsmen after continuous and intense stresses. Within the scope of rheumatology, mud-baths and balneotherapy have curative and rehabilitative potentials leading to a

reduction, and often a disappearance, of pain with a faster recovery of the locomotory system. The gastrointestinal system is a target of psychic as well as physical stresses displaying symptoms or diseases which may be favourably addressed with the aid of mineral waters. This treatment has proved effective in secretory and motility dysfunctions of the biliary tree allowing a rapid functional recovery. Mineral water treatments are successfully employed in the treatment of urologic disturbance and ORL and dermatological pathologies, where local applications such as mud baths, balneotherapy, showers and aerosols, play a critical role.

PMID:

9296924

[PubMed - indexed for MEDLINE]

## **Paper 8**

**Acta Otorhinolaryngol Ital. 1990;10 Suppl 28:23-34.  
[Anti-inflammatory drugs in ORL].**

[Article in Italian]

**Felisati D, Manghisi P.**

### **Source**

Divisione ORL Ospedale Bassini, Cinisello Balsamo, Milano.

### **Abstract**

The idea of anti-inflammatory therapy in medicine arose in the 1950's with the development of corticosteroids. Prior to this time the treatment of phlogistic pathologies was aimed at achieving analgesic, antipyretic and diaphoretic effects. Cortisone and its derivatives have spurred the setting up of a series of pharmacological tests to study their anti-inflammatory activity and to verify their clinical efficacy in rheumatology. The side effects of corticosteroids have promoted research into non steroid anti-inflammatory drugs (NADs). A new pharmacological class has been created which includes substances-some previously known and some newly synthesized-which can also be used in disease other than rheumatic pathologies. In the E.N.T. field, both cortisone (and its derivatives) and NADs have been applied in many different types of inflammatory pathologies: infective and non infective, acute, subacute, recurrent, chronic and chronic with exacerbations. Modern antiphlogistic therapy avails itself of other therapeutic means of defense as well; means such as proteolytic and secretolytic enzymes, antiedematous substances and the old sulphuric crenotherapy whose action mechanism can, today, be newly interpreted and reassessed in light of modern pharmacological knowledge.

PMID:

2248024

[PubMed - indexed for MEDLINE]

## **Paper 9**

**Am Rev Respir Dis. 1991 Jul;144(1):31-5.**

**Acute exacerbation of bronchial asthma in children associated with afternoon weather changes.**

**Beer SI, Kannai YI, Waron MJ.**

## Source

Children's Pulmonary-Allergic and Metabolic Services, Assaf Harofeh Medical Center, Zerifin, Israel.

## Erratum in

Am Rev Respir Dis 1991 Oct;144(4):995.

## Abstract

We studied the effect of the weather on acute exacerbations of bronchial asthma in children by comparing records of 8,657 admissions for five acute respiratory diseases (3,064 for asthma) with concurrent meteorologic data. These diseases were classified according to their interrelations and distinct meteorologic patterns into two groups: (1) acute asthma and acute laryngitis, which are correlated with the afternoon gradients of air temperature, heat content (the thermal energy of the ambient air), and modified heat content factor (the energy required to heat the air water vapor to the ambient temperature), but not correlated with the absolute values of air temperature and water content; and (2), bronchopneumonia/pneumonia and upper respiratory infections, which are correlated only with the absolute values of the meteorologic parameters (air temperature, water content, heat content, and modified heat content factor), but not with their afternoon gradients. Admissions for bronchiolitis revealed an age-related pattern: up to 1 yr they resembled Group 2 and from 1 to 2 yr, Group 1. It follows that the admission rates of acute exacerbation of bronchial asthma in childhood are linked both to the afternoon weather gradients and to some of the acute respiratory infections.

PMID:

2064137

[PubMed - indexed for MEDLINE]

## Paper 10

[Ann Allergy.](#) 1990 Dec;65(6):463-8.

**Effect of sulfurous (thermal) water on T lymphocyte proliferative response.**

[Valitutti S](#), [Castellino F](#), [Musiani P](#).

## Source

Department of Human Pathology, Università G. D'Annunzio, Chieti, Italy.

## Abstract

We studied the effect of sulfurous water thermal therapy on the phenotype and the proliferative response of peripheral lymphoid cells from ten subjects affected by chronic upper respiratory disease and from six suffering from articular and periarticular disorders. Sulfurous water (S-H<sub>2</sub>O) therapy did not modify the phenotype and function of peripheral blood mononuclear cells (PBMC) nor did it modify systemic immunologic reactivity. A different result was obtained by analyzing the response to mitogens of peripheral blood mononuclear cells in cell cultures containing graduated amounts of S-H<sub>2</sub>O. These "in vitro" studies have shown an important dose-dependent inhibitory effect of S-H<sub>2</sub>O on mitogen induced T lymphocyte proliferation and on IL2 production. H<sub>2</sub>S present in S-H<sub>2</sub>O seems to be the primary component responsible for inhibition. Our results are consistent with a local immunosuppressive role of S-H<sub>2</sub>O, which may explain part of the observed therapeutic effect of inhalation therapy on upper respiratory allergic disorders.

PMID:  
2256575  
[PubMed - indexed for MEDLINE]

## Paper 11

### **[Good tolerance and absence of immunologic effects in mice treated with arsenic-rich thermal water].**

[Article in French]

[Mercier P](#), [Papon E](#), [Van Den Berghe C](#), [Drutel P](#), [Rouveix B](#).

#### **Source**

Département de Pharmacologie Clinique, INSERM U13, Paris.

#### **Abstract**

Three strains of mice were given, per os and ad libitum, a spa water containing 6.8 mg/l arsenic and indicated for the treatment of allergic respiratory diseases or chronic bronchitis. The daily arsenic intake was approximately from 1.5 to 4 mg/kg. No effect on body weight gain or on the various immune parameters assessed was observed. These results demonstrate that this spa water, despite its high arsenic content, is not toxic and does not interfere with the immune system of healthy mice.

PMID:  
2148901  
[PubMed - indexed for MEDLINE]

## Paper 12

[Eur Arch Otorhinolaryngol.](#) 2013 Feb;270(2):565-70. doi: 10.1007/s00405-012-2024-5. Epub 2012 May 16.

### **SPA therapy of upper respiratory tract inflammations.**

[Passali D](#), [De Corso E](#), [Platzgummer S](#), [Streitberger C](#), [Lo Cunsolo S](#), [Nappi G](#), [Passali GC](#), [Bellussi L](#).

#### **Source**

University of Siena Medical School, Siena, Italy, d.passali@virgilio.it.

#### **Abstract**

The upper airway respiratory diseases (i.e. common cold, allergic rhinitis, nonallergic/vasomotor rhinitis, acute and chronic rhinosinusitis and nasal polyposis) in which nasal congestion is a common symptom are often undertreated due to the frequent inadequate efficacy and safety concern with current therapies. In scientific literature, few studies seem to support the hypothesis that nasal inhalatory treatment with thermal water promotes the improvement of nasal symptoms, even if the mechanisms by which the improvement from SPA therapy can be expected remain debated.

A prospective comparative study with a pre-post design has been performed consecutively enrolling 33 (males 70 %) patients of both genders older than 12 years of age, affected by chronic sinonasal inflammation. All patients underwent a 14-days course of radioactive water warm vapour inhalations

followed by nasal aerosol of the same thermal water 10 min each once/day at Merano Terme. At the beginning and end of the study, in all the subjects, nasal function evaluation by active anterior rhinomanometry, mucociliary transport time (MCTt) determination and nasal cytology were performed.

After the inhalatory treatment, the mucociliary function was improved and the pathologic mucociliary transport times recorded at the beginning of the study being significantly reduced to physiologic ones. Besides, before treatment, the cytologic picture showed an inflammatory cell infiltration (eosinophils, neutrophils with/without bacteria, mast cells) in 37 % of patients; after therapy in 66 % of these patients, the rhinocytogram was normal. Our results suggest, according to the literature data, that SPA therapy with radioactive water could represent an alternative choice in chronic inflammatory diseases of the upper airways, nonresponsive to pharmacological therapy.

PMID: 22588193

[PubMed - in process]

### **Paper 13**

[Exp Lung Res.](#) 2012 Mar;38(2):67-74. doi: 10.3109/01902148.2011.641668. Epub 2011 Dec 20.

#### **Free radical-scavenging activity of sulfurous water investigated by electron paramagnetic resonance (EPR) spectroscopy.**

[Braga PC](#), [Dal Sasso M](#), [Culici M](#), [Falchi M](#), [Spallino A](#), [Nappi G](#).

#### **Source**

Center of Respiratory Pharmacology, Department of Pharmacology, School of Medicine, University of Milan, Milan, Italy. piercarlo.braga@unimi.it

#### **Abstract**

The aim of the study was to explore the antiradical activity of sulfurous water, used for inhalatory therapy (characterized by the presence of sulfhydryl [HS]) by means of electron paramagnetic resonance (EPR) spectroscopy. The effects of sulfurous water corresponding to the concentrations from 16 down to 0.25 µg/mL of HS were tested by means of Fenton reaction (HO•), KO<sub>2</sub>-crown ether system (O<sub>2</sub>-•), and EPR of Tempol and of Fremy's salt radical. All of these assays were made using natural sulfurous water or degassed sulfurous water (no detectable HS) or reconstituted sulfurous water (degassed plus NaHS). The free radicals were significantly inhibited by natural water with HS concentrations ranging from 16 to 1 µg/mL for HO•, Tempol, and Fremy's salt, and O<sub>2</sub>-• was significantly inhibited from 16 and 2 µg/mL. The tests of degassed water did not reveal any significant differences from baseline values. The tests of reconstituted water led to significant results overlapping those obtained using natural water, thus confirming the importance of the presence of HS group (reductive activity). The positive effects of the activity of sulfurous thermal water is partially based on the patients' subjective sense of well-being and partially on symptomatic (or general) clinical improvements that are sometimes difficult to quantify. These findings indicate that, in addition to their known mucolytic activity and trophic effects on respiratory mucosa, the HS groups in sulfurous water also have antioxidant activity that contributes to the water's therapeutic effects on upper and lower airway inflammatory diseases.

PMID:

22185392

[PubMed - indexed for MEDLINE]



## Paper 14

[Ther Adv Respir Dis.](#) 2010 Dec;4(6):333-40. doi: 10.1177/1753465810376783. Epub 2010 Jul 22.

### Effects of sulphurous water on human neutrophil elastase release.

[Braga PC](#), [Dal Sasso M](#), [Culici M](#), [Spallino A](#), [Marabini L](#), [Bianchi T](#), [Nappi G](#).

#### Source

Center of Respiratory Pharmacology, Department of Pharmacology, School of Medicine, University of Milan, Via Vanvitelli 32, 20129 Milan, Italy. piercarlo.braga@unimi.it

#### Abstract

##### **BACKGROUND:**

Molecules bearing a sulphide (HS) group, such as glutathione, play a fundamental role in the defensive system of human airways, as shown by the fact that the lining fluid covering the epithelia of the respiratory tract contains very high concentrations of glutathione: the lungs and nose, respectively, contain about 140 and 40 times the concentrations found in plasma. Consequently, various low-weight soluble molecules bearing an HS group (including N-acetylcysteine, mesna and thiopronine, and prodrugs such as stepronine and erdosteine) have been used for therapeutic purposes. HS groups can also be therapeutically administered by means of sulphurous thermal water containing HS groups. The aim of this study was to investigate the direct activity of such water on the release of elastase by activated human neutrophils.

##### **METHOD:**

After the neutrophils were incubated with increasing amounts of sulphurous water or the HS/hydrogen sulphide donor sodium hydrosulphide (NaHS), elastase release was initiated by N-formyl-methionyl-leucyl-phenylalanine and measured by means of spectrofluorimetry using methylsuccinylalanylprolylvalyl-methylcoumarin amide as the fluorogenic substrate. To verify the presence of direct action on elastase we determined the diameter of the area of elastinolysis on elastine-agarose gel plates.

##### **RESULTS:**

The sulphurous water significantly inhibited elastase release at HS concentrations ranging from 4.5 to 18 µg/ml, as assayed using the iodometric method; in the case of NaHS, the inhibition was significant at HS concentrations ranging from 2.2 to 18 µg/ml. The concentration-effect regression lines of both were parallel and neither showed any direct elastolytic activity.

##### **CONCLUSIONS:**

Previous claims concerning the activity of sulphurous water have been based on the patients' subjective sense of wellbeing and on symptomatic (or general) clinical improvements that are not easy to define or quantify exactly. Our findings indicate that, in addition to its known mucolytic and antioxidant activity, sulphurous water also has an anti-elastase activity that may help to control the inflammatory processes of upper and lower airway diseases.

PMID:

20650977

[PubMed - indexed for MEDLINE]

## Paper 15

[Respiration](#). 2008;75(2):193-201. Epub 2007 Sep 5.

### Antioxidant effect of sulphurous thermal water on human neutrophil bursts: chemiluminescence evaluation.

[Braga PC](#), [Sambataro G](#), [Dal Sasso M](#), [Culici M](#), [Alfieri M](#), [Nappi G](#).

#### Source

Center of Respiratory Pharmacology, Department of Pharmacology, School of Medicine, University of Milan, Milan, Italy. piercarlo.braga@unimi.it

#### Abstract

##### **BACKGROUND:**

The activities of the HS (sulfhydryl or thiolic) group in the cysteine of glutathione or various low-weight soluble molecules (thiolic drugs), such as N-acetylcysteine, mesna, thiopronine and dithiotreitol or stepronine and erdosteine (prodrugs), include its antioxidant activity in the airways during the release of reactive oxygen or nitrogen species (ROS, RNS) by polymorphonuclear neutrophils (PMNs) activated in response to exogenous or endogenous stimuli.

##### **OBJECTIVE:**

In addition to being administered by means of thiolic molecules, the HS group can also be given by means of the inhalation of sulphurous thermal water. The aim of this study was to investigate the effect of sulphurous thermal water on the release of ROS and RNS during the bursts of human PMNs.

##### **METHODS:**

The luminol-amplified chemiluminescence methodology was used to investigate the ROS and RNS released by PMNs stimulated with N-formyl-methionyl-leucyl-phenylalanine and phorbol-12-myristate-13-acetate, before and after incubation with sulphurous water. Effects on cell-free systems were also investigated.

##### **RESULTS:**

The water significantly reduced the luminol-amplified chemiluminescence of N-formyl-methionyl-leucyl-phenylalanine- and phorbol-12-myristate-13-acetate-activated PMNs on average from 0.94 to 15.5 mug/ml of HS, even after the addition of L-arginine, a nitric oxide (NO) donor. Similar findings have also been obtained in a cell-free system, thus confirming the importance of the presence of the HS group (reductive activity).

##### **CONCLUSIONS:**

The positive effects of the activity of sulphurous thermal waters has been partially based on the patients' subjective sense of wellbeing and partially on not always easy to quantify symptomatic (or general) clinical improvements. Our findings indicate that, in addition to their known mucolytic activity and trophic effects on respiratory mucosa, the HS groups present in the sulphurous thermal water of this spring also have antioxidant activity that contributes to the therapeutic effects of the water in upper and lower airway inflammatory diseases.

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PMID: 17804898

## Paper 16

[Respir Med](#). 2005 Jun;99(6):748-54. Epub 2004 Dec 13.

## Effect of inhalation of thermal water on airway inflammation in chronic obstructive pulmonary disease.

[Pellegrini M](#), [Fanin D](#), [Nowicki Y](#), [Guarnieri G](#), [Bordin A](#), [Faggian D](#), [Plebani M](#), [Saetta M](#), [Maestrelli P](#).

### **Source**

Department of Environmental Medicine and Public Health, University of Padova, via Giustiniani, 2 35128 Padova (PD), Italy.

### **Abstract**

Thermal water inhalations have been traditionally used in the treatment of upper and lower chronic airway diseases. However, the benefit and the mechanism of this treatment have not been properly assessed. To determine whether inhaled salt-bromide-iodine thermal water improves lung function, quality of life and airway inflammation, 39 patients with chronic obstructive pulmonary disease (COPD) were randomly assigned to receive 2-weeks inhalation treatment with thermal water (active, no. = 20) or normal saline (control, no. = 19) in single blind. Lung volumes were measured, Saint George's respiratory questionnaire (SGRQ) was administered and induced sputum was performed before and after treatment. No changes in pre- and post-salbutamol lung volumes was observed after inhalation treatment in both groups. SGRQ score showed a significant improvement in active group compared with control group at the end of the trial. The concentration of total cells in induced sputum increased significantly in both active ( $P < 0.05$ ) and control groups ( $P < 0.05$ ). Inhalation of thermal water induced a small but significant decrease in percentages of sputum neutrophils ( $P < 0.01$ ) and a parallel increase in macrophages ( $P < 0.01$ ). In contrast, normal saline inhalation was not associated with changes in differential sputum cell counts. In conclusion, treatment with inhaled salt-bromide-iodine thermal water in COPD is associated with a reduced proportion of neutrophils in induced sputum suggesting that thermal water may have a mild anti-inflammatory effect on the airways. However, the short-term improvement in some components health-related quality of life was not related with changes in lung function or with the degree of airway inflammation.

PMID: 15878492

[PubMed - indexed for MEDLINE]

### **Paper 17**

[Exp Biol Med \(Maywood\)](#). 2003 Nov;228(10):1245-9.

## Clinical implications of thermal therapy in lifestyle-related diseases.

[Biro S](#), [Masuda A](#), [Kihara T](#), [Tei C](#).

### **Source**

Department of Cardiovascular, Respiratory and Metabolic Medicine, Graduate School of Medicine, Kagoshima University, Kagoshima 890-8520, Japan.

### **Abstract**

Systemic thermal therapy, such as taking a warm-water bath and sauna, induces systemic vasodilation. It was found that repeated sauna therapy (60 degrees C for 15 min) improved hemodynamic parameters, clinical symptoms, cardiac function, and vascular endothelial function in patients with congestive heart failure. Vascular endothelial function is impaired in subjects with lifestyle-related

diseases, such as hypertension, hyperlipidemia, diabetes mellitus, obesity, and smoking. Sauna therapy also improved endothelial dysfunction in these subjects, suggesting a preventive role for atherosclerosis. In animal experiments, sauna therapy increases mRNA and protein levels of endothelial nitric oxide synthase (eNOS) in aortas. In normal-weight patients with appetite loss, repeated sauna therapy increased plasma ghrelin concentrations and daily caloric intake and improved feeding behavior. In obese patients, the body weight and body fat significantly decreased after 2 weeks of sauna therapy without increase of plasma ghrelin concentrations. On the basis of these data, sauna therapy may be a promising therapy for patients with lifestyle-related diseases.

PMID: 14610268

[PubMed - indexed for MEDLINE]

## Paper 18

[Pediatrie](#). 1990;45(11):769-74.

### [Treatment of respiratory and ORL diseases with mineral waters in children].

[Article in French]

[Fauquet JL](#), [Labbé A](#).

## Source

Hôpital thermal pour enfants Guillaume-Lacoste, La Bourboule, France.

## Abstract

Many questions arise when a paediatrician prescribes thermal treatment. Answers to these questions have come to light in recent literature. For paediatric indications, thermal treatment is dominated by asthma and its allergic equivalents. In such cases, sodium chloride and bicarbonated spas are used. Such indications are based on the research of the Pasteur Institute for Le Mont-Dore spa and on different modifications of intracellular enzymes and increase of resistance to hypoxia incited by the La Bourboule spa. The waters in the spas of the Pyrenees contain sulphur, and are mainly used for the treatment of chronic or repeated ENT infections. Fundamental studies in favour of thermal treatment have only aroused indirect views. Following the enquiry made by the French National Health Service on 3,000 patients over a period of 3 years from 1983, it was found that this treatment reduces medical consumption, doctor's visits and hospital care in many cases. However no double-blind research could be performed despite the desire of several spas. These spas improve either the quality of the final product or the strict hygiene level in the thermal installations, and also the sanitary educational measures associated with thermal treatment.

PMID: 2177879

[PubMed - indexed for MEDLINE]

## Paper 19

[C R Seances Soc Biol Fil](#). 1990;184(2):164-74.

### [Good tolerance and absence of immunologic effects in mice treated with arsenic-rich thermal water].

[Article in French]

[Mercier P](#), [Papon E](#), [Van Den Berghe C](#), [Drutel P](#), [Rouveix B](#).

## Source

Département de Pharmacologie Clinique, INSERM U13, Paris.

## Abstract

Three strains of mice were given, per os and ad libitum, a spa water containing 6.8 mg/l arsenic and indicated for the treatment of allergic respiratory diseases or chronic bronchitis. The daily arsenic intake was approximately from 1.5 to 4 mg/kg. No effect on body weight gain or on the various immune parameters assessed was observed. These results demonstrate that this spa water, despite its high arsenic content, is not toxic and does not interfere with the immune system of healthy mice.

PMID: 2148901

[PubMed - indexed for MEDLINE]

## Paper 20

Am J Rhinol Allergy. 2012 Jan-Feb;26(1):e15-9. doi: 10.2500/ajra.2012.26.3733.

### [Crenotherapy modulates the expression of proinflammatory cytokines and immunoregulatory peptides in nasal secretions of children with chronic rhinosinusitis.](#)

Passariello A, Di Costanzo M, Terrin G, Iannotti A, Buono P, Balestrieri U, Balestrieri G, Ascione E, Pedata M, Canani FB, Canani RB.

Department of Pediatrics, University of Naples Federico II, Via S. Pansini 5, Naples, Italy.

**BACKGROUND:** The effect of crenotherapy on major mucosal markers of inflammation,

TNF alpha, human beta-defensins 2 (hBD-2), and calprotectin, are largely unexplored in pediatric chronic rhinosinusitis (CRS). The aim of this study was to investigate the effects of crenotherapy with sulfate-sodium-chloride water on mucosal markers of inflammation in children with CRS.

**METHODS:** Children with CRS received 15-day crenotherapy consisting of sulfate-sodium-chloride thermal water inhalations by nasal aerosol (15 minutes/day). Concentrations of nasal mucosal markers of inflammation (TNF alpha, hBD-2, and calprotectin) were measured before and after crenotherapy. Presence of

specific symptoms (nasal obstruction, nasal discharge, facial pain, sense of smell, and cough), value of symptoms score sino-nasal 5 (SN5), quality of life (QoL) score (1 [worse] to 10 [optimal]) were also assessed.

**RESULTS:** After crenotherapy a significant reduction was observed in TNF alpha

(from  $0.14 \pm 0.02$  to  $0.08 \pm 0.01$ ;  $p < 0.001$ ), calprotectin (from  $2.9 \pm 1.0$  to  $1.9 \pm 0.5$ ;  $p < 0.001$ ), and hBD-2 (from  $2.0 \pm 0.1$  to  $0.9 \pm 0.6$ ;  $p < 0.001$ )

concentrations. A significant ( $p < 0.05$ ) reduction in number of subjects presenting symptoms of nasal obstruction (100% versus 40%), nasal discharge (33% versus 13%), facial pain (30% versus 10%), and sense of smell (60% versus 20%)

was observed. A significant improvement of SN5 (from  $3.07 \pm 0.76$  to  $2.08 \pm 0.42$ ;

$p < 0.001$ ) was observed after the crenotherapy. QoL also improved after crenotherapy (from  $4.2 \pm 1.1$  to  $6.6 \pm 1.0$ ;  $p < 0.001$ ).

## CONCLUSION:

Crenotherapy induced a down-regulation of nasal mucosal inflammatory mediators in children with CRS.

PMID: 22391070 [PubMed - indexed for MEDLINE]

## Paper 21

Int J Immunopathol Pharmacol. 2011 Oct-Dec;24(4):1103-9.

### Effectiveness of Ischia thermal water nasal aerosol in children with seasonal allergic rhinitis: a randomized and controlled study.

Miraglia Del Giudice M, Decimo F, Maiello N, Leonardi S, Parisi G, Golluccio M, Capasso M, Balestrieri U, Rocco A, Perrone L, Ciprandi G.

Allergic rhinitis is characterized by local inflammation. Nasal lavage may be a useful treatment, however, there are few studies on this topic. This study aims to evaluate the effects of Ischia thermal water nasal irrigation on allergic rhinitis symptoms and airway inflammation during the period of natural exposure to Parietaria pollen in children with allergic rhinitis and intermittent asthma.

Forty allergic children were randomly divided into two groups: the first group (Group 1) practiced crenotherapy with thermal water aerosol for 15 days per month, for three consecutive months, the control group (Group 2) was treated with

0.9% NaCl (isotonic) solution. In addition, all children were treated with cetirizine (0.5 gtt./kg/day once daily). Nasal symptom assessment, including Total Symptom Score (TSS), spirometry, and exhaled nitric oxide (FeNO) were considered before the treatment (T0), at the end of the treatment (T1) and again 2 weeks after the end of the treatment (T2). The study was registered in the Clinical Trials.gov (NCT01326247). Thermal water significantly reduced both TSS and FeNO levels and there was a significant relationship between reduction of nasal symptoms and FeNO values at the end of treatment with thermal water. In conclusion, this study shows that nasal crenotherapy with the hypermineral chloride-sodium water of Ischia was effective in children with seasonal allergic rhinitis based on the sensitivity to Parietaria. These results demonstrate that this natural treatment may be effective in a common and debilitating disease such as the allergic rhinitis.

PMID: 22230419 [PubMed - indexed for MEDLINE]

## Paper 22

Int J Biometeorol. 2010 Sep;54(5):491-3. doi: 10.1007/s00484-010-0311-7. Epub 2010 Mar 29.

### Crenotherapy: a neglected resource for human health now re-emerging on sound scientific concepts.

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Recent mechanistic evidence demonstrates that spa-based therapy (or, as we propose, crenotherapy from the Greek word kapparhoepsilonnueta, spring fountain)

is indeed based on solid scientific data. This mini-review highlights the latest insights into the mechanisms of crenotherapy derived from in vitro experiments, studies on animal models, and carefully designed clinical trials. Although more

basic and clinical data are still needed, crenotherapy is coming of age as a modern, scientifically sound therapy. As the underlying mechanisms are uncovered, it is becoming possible to choose the most appropriate applications of this centuries-old practice, possibly reducing medical costs, thus explaining the current worldwide renewed interest in crenotherapy.  
PMID: 20349352 [PubMed - indexed for MEDLINE]

### **Paper 23**

Clin Ter. 2009;160(1):17-20.

#### **Clinical study on 40 cases of inflammatory pathologies of upper respiratory and digestive tract treated by inhalatory crenotherapy.**

[Article in Italian]

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**OBJECTIVES:** Authors present beneficial effects of crenotherapy on 40 patients suffering from inflammatory mucosal conditions of upper respiratory-digestive tract (URDT).

**MATERIALS AND METHODS:** Our study was realized at the hydrothermal premises in

Telesse Terme (BN, Italy). Subjects selected for this study are 40 patients (22 males and 18 females) aged 20-68 years (mean 38.6 years) who suffered from catarrhal and inflammatory mucosal diseases of URDT. The patients, who are informed about the modalities of the study, undergo E.N.T. examination and nasal mucosal brushing for cytologic analysis before and after crenotherapy.

### **RESULTS**

At the end of the therapeutic course we observed a relevant improvement of clinical indicators and of mucociliary transport time in URDT. Moreover, a satisfactory control of local inflammation is highlighted by a rhinocytogram, performed after crenotherapy and showing an increase in plasma cells, a decrease in granulocytes and a normalization of mucous secretion (nasal mucosal histology).

### **CONCLUSION**

Our study shows that sulphurous waters are particularly effective in anti-catarrhal and anti-inflammatory therapy of URDT.  
PMID: 19290407 [PubMed - indexed for MEDLINE]

### **Paper 24**

Clin Ter. 2008 May-Jun;159(3):175-80.

#### **[Efficacy of inhalation therapy with water of Salsomaggiore (Italy) in chronic and recurrent nasosinusal inflammation treatment].**

[Article in Italian]

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OBJECTIVES: Aim of the research was the demonstration of the efficacy of thermal

water vs saline in the recurrent and chronic nasosinusal pathologies treatment.

## **MATERIALS AND METHODS**

120 patients randomized into 2 groups of 60 subjects each, all affected by recurrent or chronic rhinosinusitis with/without I degree nasal polyposis. At the beginning and at the end of the study, in all the subjects the clinical history, objective examination and the instrumental analysis of nasal functions by active anterior rhinometry, acoustic rhinometry, nasal mucociliary transport time determination and nasal mucosa scraping were performed.

Patients of the study group underwent crenotherapy treatment (vapour inhalation, aerosol and nasal douching) with thermal water for 14 days at Salsomaggiore Thermal baths. Other patients underwent nasal douching and aerosol with saline twice a day for 14 days at the Rhinologic Centre of the ENT Clinic of Siena University.

## **RESULTS**

At the end of the study, only the patients undergone to crenothrapic treatment with salt-bromine-iodic water showed a significant improvement of nasal

obstruction, rinorrea and number of nocturnal arousals. The improvement, even if present, was not significant in the control group. Same positive variations were observed concerning nasal mucosa congestion, nasal secretion and mucociliary transport time reaching the significance in the study group.

## **CONCLUSIONS**

Crenotherapy with salt-bromine-iodic water should be considered as efficacious therapeutic tool in the management of chronic and recurrent rhinosinusitis.

PMID: 18594748 [PubMed - indexed for MEDLINE]

### **Paper 25**

CLINICAL AND EXPERIMENTAL OTORHINOLARYNGOLOGY Volume: 6  
Issue: 1 Pages: 7-11 DOI: 10.3342/ceo.2013.6.1:7 Published: MAR 2013

## **Impact of sulphurous water Politzer inhalation on audiometric parameters in children with otitis media with effusion**

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### **Objectives.**

The positive effects of spa therapy on ear, nose, and throat pathology are known but robust literature in this field, is still lacking. The aim of this study was to assess through a retrospective analysis, the effects on otitis media with effusion of Politzer endotympanic inhalation of sulphurous waters in children aged 5-9 years.

### **Methods.**

A cohort of 95 patients was treated with Politzer insufflations of sulphurous water: 58 patients did a cycle consisting of a treatment of 12 days per year for



three consecutive years; 37 patients followed the same procedure for 5 years consecutively. The control population was represented by untreated, age-matched children. A standard audiometric test was used before and after each cycle of treatment.

### **Results.**

One cycle of Politzer inhalation of sulphur-rich water improved the symptoms. Three cycles definitively stabilind the improvement of hearing function.

Conclusion. Our results show that otitis media with effusion in children can be resolved by an appropriate non-pharmacological treatment of middle ear with sulphur-rich water.